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Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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Overview for Request: cder_mpl2p_wp021

Request ID: cder_mpl2p_wp021

<u>Request Description:</u> In this request, we assessed the risk of angioedema associated with sacubitril/valsartan (SV) compared to angiotensin-converting enzyme inhibitors (ACEIs) or to angiotensin II receptor blockers (ARBs, excluding SV) among heart failure patients in the Sentinel Distributed Database (SDD).

<u>Sentinel Routine Querying Module:</u> Cohort Identification and Descriptive Analysis (CIDA) and Propensity Score Analysis (PSA) tools, version 9.7.0, with ad hoc programming

<u>Data Source:</u> The study period spanned from July 7, 2015 to February 29, 2020. We distributed the analytic package to five Data Partners (DP) on January 13, 2021. This report contains aggregated data from five DPs for which the propensity score estimation models converged across all comparisons. See Appendix A for a list of the latest dates of available data for each DP included in this report.

<u>Study Design:</u> We identified individuals with incident use of SV, ACEIs, and ARBs who were 18 years or older with a history of heart failure and evaluated the occurrence of angioedema and serious angioedema during exposure episodes. We then conducted a PSA comparing the SV users to the ACEI or ARB users, matching and stratifying on propensity score. This is a Type 2 analysis using the Propensity Score Analysis module in the Query Request Package (QRP) documentation.

<u>Exposure and Comparator:</u> We defined exposures of interest as new use of SV, ACEIs, and ARBs. The exposure drugs were defined using National Drug Codes (NDCs). For a list of generic and brand names of medical products used to define the exposure and comparator drugs, please see Appendix B.

<u>Outcomes of Interest:</u> We defined our main outcome of interest, angioedema, as an angioedema diagnosis code recorded in any diagnostic position of an inpatient, emergency department, or outpatient encounter. We defined our secondary outcome of interest, serious angioedema, as an angioedema diagnosis recorded in any diagnostic position of an inpatient or emergency department encounter with evidence of an intensive care unit admission, intubation, tracheostomy, or laryngoscopy occurring within two days of the hospital admission or emergency department visit. We defined our outcomes using International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS). For a list of codes used to define outcomes, please see Appendix C.

Cohort Eligibility Criteria: We required patients 18 years or older to be enrolled in plans with both medical and drug coverage for at least 183 days before index dispensing, during which gaps in coverage of up to 45 days were allowed and treated as continuous enrollment. New use of ACEI or ARB was defined as no use of SV, ACEIs, or ARBs in the 183 days preceding the index dispensing (index date). New use of SV was defined as no use of SV in the 183 days preceding the index date, in addition to prior or ongoing use of the comparator (ACEIs or ARBs, evidenced by dispensing date or days supply) in the 183 days preceding and including the index date; a sensitivity analysis alternatively required prior or ongoing use of the comparator in the 14 days preceding and including the index date. We included patients with evidence of heart failure in the 183 days preceding and including index date. We excluded patients from the cohort if they had evidence of a dispensing for the other two exposures on their index date. Incidence, inclusion, and exclusion criteria were defined using ICD-9-CM and ICD-10-CM diagnosis codes. For a list of generic and brand names of medical products and specific diagnosis codes used to define cohort eligibility, please see Appendices D and E.

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Follow-up: We determined follow-up time based on the length of the exposure episodes and censored upon prespecified criteria. We created exposure episodes using outpatient pharmacy dispensing data. We bridged together exposure episodes less than 14 days apart and added 14 days at the end of each exposure episodes to create continuous treatment episodes. A sensitivity analysis shortened the episode gap and episode extension to 7 days. Follow-up began on the day of exposure initiation and continued until the earliest of any of the following: 1) outcome occurrence; 2) requester-defined censoring criteria -- initiation of any of the other two study drugs or after 365 days of continuous exposure; 3) disenrollment; 4) recorded death; 5) end of exposure episode; 6) end of query period; or 7) end of available data. Only the first valid exposure episode that occurred during the study period was included per patient, with the exception for one-time cohort reentry from the comparator to SV group upon initiation of SV during the first comparator exposure episode plus when new use criteria of SV was satisfied.

<u>Baseline Covariates:</u> Please refer to Appendices F, G, and I for a list of covariates, codes, and evaluation windows used to defined covariates.

Propensity Score Estimation: For each comparison, we fit a logistic regression model to estimate the propensity score (PS) based on potential confounders and risk factors outlined in Appendix J. The matching ratio for the PS was 1:1 and the matching caliper was 0.05. Exposure and comparator episodes were nearest neighbor-matched without replacement. We also used PS stratification (deciles) for our main analyses comparing SV to ACEIs and ARBs and risk of angioedema. For each comparison, we used risk set-based approach to estimate the hazard ratio and 95% confidence intervals for the unadjusted analyses, unconditional and conditional matched analyses, and PS-stratified analyses. Subgroup analyses for effect estimation included angioedema diagnosis in 183 days prior to index date and separately, angioedema diagnosis in entire enrollment history prior to index date; serious allergies diagnosis in the 183 days prior to index date; sex; age group; race; and follow-up time.

See Appendices H and I for the specifications of parameters used in the analyses for this request.

<u>Limitations:</u> As with all observational studies, this evaluation was limited in its ability to control for all sources of potential bias. Algorithms used to define exposures, outcomes, inclusion and exclusion criteria, and covariates are imperfect and may be misclassified. Therefore, data should be interpreted with this limitation in mind.

<u>Notes:</u> Please contact the e Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's routine querying modules, please refer to the documentation (https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-queryingtooldocumentation/browse).

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Glossary of Terms for Analyses Using Cohort Identification and Descriptive Analysis (CIDA) Module*

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.

Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

Ambulatory Visit (AV) - includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.

Emergency Department (ED) - includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.

Inpatient Hospital Stay (IP) - includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.

Non-Acute Institutional Stay (IS) - includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.

Other Ambulatory Visit (OA) - includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Charlson/Elixhauser Combined Comorbidity Score - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).

Code Days - the minimum number of times the diagnosis must be found during the evaluation period in order to fulfill the algorithm to identify the corresponding patient characteristic.

Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.

Computed Start Marketing Date - represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.

Eligible Members - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

Event Deduplication - specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.

Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

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Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.

Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be considered.

Minimum Episode Duration - specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.

Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

Query Period - period in which the modular program looks for exposures and outcomes of interest.

Switch Evaluation Step Value - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).

Switch Gap Inclusion Indicator - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.

Switch Pattern Cohort Inclusion Date - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.

Switch Pattern Cohort Inclusion Strategy - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.

Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.

Washout Period (drug/exposure) - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

Washout Period (event/outcome) - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*all terms may not be used in this report

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Glossary of Terms for Analyses Using Propensity Score Analysis (PSA) Tool*

Covariate - requester defined binary variable to include in the propensity score estimation model (e.g., diabetes, heart failure, etc.) during requester-defined lookback period. Requester may also choose to add any of the following categorical, continuous, or count

- 1. Age (continuous)
- 2. Sex
- 3. Time period (i.e., monitoring period for sequential analyses)
- 4. Year of exposure
- 5. Comorbidity score
- 6. Medical utilization number of inpatient stays
- 7. Medical utilization number of institutional stays
- 8. Medical utilization number of emergency department visits
- 9. Medical utilization number of outpatient visits
- 10. Health care utilization number of other ambulatory encounters (e.g., telemedicine, email consults)
- 11. Drug utilization number of dispensings
- 12. Drug utilization number of unique generics dispensed
- 13. Drug Utilization number of unique drug classes dispensed

Covariate Evaluation Window - specified number of days relative to index date to evaluate the occurrence of covariates of interest. Note: members are required to have continuous enrollment during the covariate evaluation window, regardless of the value Individual Level Data Return - program may return individual-level, de-identified datasets to the Sentinel Operations Center (SOC). While the datasets contain a single row per patient for each specified analysis, patient identifiers such as a patient ID are not included in the output. Individual-level datasets are returned to the SOC, aggregated, and used to calculate effect estimates via Cox Mahalanobis Distance - provides a measure of balance across all variables while accounting for their correlation.

Matching Caliper - maximum allowed difference in propensity scores between treatment and control patients. Requester may select any caliper (e.g., 0.01, 0.025, and 0.05).

Matched Conditional and Unconditional Analysis - in a conditional matched analysis, a Cox model, stratified by Data Partner site and matched set, is run on the matched population. This can be done for both the both 1:1 and 1:n matched cohorts. In an unconditional analysis, a Cox model, stratified by Data Partner site only, is run on the matched population. This can be done for the Propensity Score Stratification - option to stratify propensity scores based on requester-defined percentiles in the unmatched population. In a stratified analysis, a Cox model, stratified by Data Partner site, is run on the stratified population. Note that all PSM Tool - performs effect estimation by comparing exposure propensity-score matched parallel new user cohorts. Propensity score estimation and matching are conducted within each Sentinel Data Partner site via distributed programming code; data are Risk-set Level Data Return - alternative to the patient-level data return approach. In this approach, the PSM tool will produce deidentified, risk-set level datasets instead of or in addition to individual-level output. Whereas each observation in the patient-level datasets represents one patient in the cohort, each observation in the risk set dataset represents one event. Risk sets are created at the Data Partner site. returned to the SOC. aggregated. and used to calculate effect estimates via case-centered logistic regression. Subgroup Analysis - may be conducted using any requester-defined covariates. Subgroup analyses may be performed in the Zero Cell Correction - indicator for whether to screen variables with a zero correction added to each cell in the confounder/outcome 2x2 table. Recommended when the number of exposed outcomes is fewer than 150.

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^{*}all terms may not be used in this report



Table 1a. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical	Covariate Balance			
	9	SV	А	CEI		
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent 100.0%	Difference	Difference
Patients (Number)	69,639	100.0%	694,882		-	-
Down a group hiss	Mann	Standard	Mann	Standard		
Demographics Mean age (years)	70.2	Deviation 11.2	Mean 72.7	Deviation 12.5	-2.563	-0.216
Age	Number	Percent	Number		-2.303	-0.210
18-44 years	2,412	3.5%	21,587	Percent 3.1%	0.357	0.020
45-54 years	5,115	7.3%	45,057	6.5%	0.861	0.034
55-64 years	11,494	16.5%	97,244	14.0%	2.511	0.070
65+ years	50,618	72.7%	530,994	76.4%	-3.729	-0.086
Sex	30,010	, 2., , ,	330,331	7 0. 170	5.725	0.000
Female	21,199	30.4%	341,867	49.2%	-18.757	-0.390
Male	48,440	69.6%	353,015	50.8%	18.757	0.390
Race	.5,	55.675	333,023	33.370	20.707	0.000
American Indian or Alaska Native	242	0.3%	4,525	0.7%	-0.304	-0.043
Asian	666	1.0%	7,871	1.1%	-0.176	-0.017
Black or African American	9,015	12.9%	92,098	13.3%	-0.308	-0.009
Native Hawaiian or Other Pacific Islander	66	0.1%	741	0.1%	-0.012	-0.004
Unknown	11,656	16.7%	99,645	14.3%	2.398	0.066
White	47,994	68.9%	490,002	70.5%	-1.598	-0.035
Hispanic Origin	1,351	1.9%	15,586	2.2%	-0.303	-0.021
Year						
2015	1,349	1.9%	87,092	12.5%	-10.596	-0.418
2016	10,510	15.1%	172,880	24.9%	-9.787	-0.247
2017	16,864	24.2%	156,573	22.5%	1.684	0.040
2018	19,077	27.4%	142,979	20.6%	6.818	0.160
2019	21,511	30.9%	133,608	19.2%	11.662	0.272
2020	328	3.6%	1,750	2.4%	1.194	0.070
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.2	2.7	5.8	3.0	-0.610	-0.214
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	33,754	48.5%	320,699	46.2%	2.318	0.046
Angioedema (-183, -1)	83	0.1%	864	0.1%	-0.005	-0.001
Angioedema (ever, -1)	494	0.7%	7,317	1.1%	-0.344	-0.037
Diabetes	35,071	50.4%	326,005	46.9%	3.446	0.069
Ischemic heart disease	55,067	79.1%	432,968	62.3%	16.767	0.375
Renal disorders	27,364	39.3%	289,746	41.7%	-2.403	-0.049
Serious allergies	8,047	11.6%	110,960	16.0%	-4.413	-0.128

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Table 1a. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

	Medical Product				Covariate Balance	
	sv		ACEI			
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	28,444	40.8%	252,983	36.4%	4.438	0.091
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	60,338	86.6%	458,102	65.9%	20.719	0.502
Everolimus	11	0.0%	183	0.0%	-0.011	-0.007
Nonsteroidal anti-inflammatory drugs (NSAIDs)	7,793	11.2%	88,957	12.8%	-1.611	-0.050
Sirolimus	****	****	208	0.0%	-0.018	-0.013
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.9	13.7	17.4	19.7	0.531	0.031
Mean number of emergency room encounters	0.7	1.4	0.9	1.8	-0.188	-0.115
Mean number of inpatient hospital encounters	0.8	1.1	1.0	1.2	-0.211	-0.186
Mean number of non-acute institutional encounters	0.2	0.8	0.4	1.1	-0.217	-0.235
Mean number of other ambulatory encounters	8.1	12.2	12.8	18.0	-4.732	-0.308
Mean number of filled prescriptions	31.3	19.8	26.9	23.0	4.408	0.205
Mean number of generics	13.1	5.1	11.5	5.7	1.614	0.297
Mean number of unique drug classes	11.4	4.5	10.8	5.0	0.626	0.131

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1b. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

	Medical Product			Covariate Balance		
	SV ACEI			CEI		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Patients (Number)	69,639	100.0%	69,639	10.0%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	70.2	11.2	70.2	12.2	-0.019	-0.002
Age	Number	Percent	Number	Percent		
18-44 years	2,412	3.5%	2,717	3.9%	-0.438	-0.024
45-54 years	5,115	7.3%	5,694	8.2%	-0.831	-0.032
55-64 years	11,494	16.5%	11,900	17.1%	-0.583	-0.016
65+ years	50,618	72.7%	49,328	70.8%	1.852	0.044
Sex						
Female	21,199	30.4%	21,398	30.7%	-0.286	-0.006
Male	48,440	69.6%	48,241	69.3%	0.286	0.006
Race						
American Indian or Alaska Native	242	0.3%	242	0.3%	0.000	0.000
Asian	666	1.0%	662	1.0%	0.006	0.001
Black or African American	9,015	12.9%	9,043	13.0%	-0.040	-0.001
Native Hawaiian or Other Pacific Islander	66	0.1%	75	0.1%	-0.013	-0.004
Unknown	11,656	16.7%	11,662	16.7%	-0.009	-0.000
White	47,994	68.9%	47,955	68.9%	0.056	0.001
Hispanic Origin	1,351	1.9%	1,521	2.2%	-0.244	-0.017
Year						
2015	1,349	1.9%	1,255	1.8%	0.135	0.010
2016	10,510	15.1%	10,469	15.0%	0.059	0.002
2017	16,864	24.2%	16,928	24.3%	-0.092	-0.002
2018	19,077	27.4%	19,069	27.4%	0.011	0.000
2019	21,511	30.9%	21,555	31.0%	-0.063	-0.001
2020	328	3.6%	363	4.0%	-0.385	-0.020
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.2	2.7	5.2	2.6	-0.017	-0.006
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	33,754	48.5%	33,596	48.2%	0.227	0.005
Angioedema (-183, -1)	83	0.1%	92	0.1%	-0.013	-0.004
Angioedema (ever, -1)	494	0.7%	723	1.0%	-0.329	-0.035
Diabetes	35,071	50.4%	34,906	50.1%	0.237	0.005
Ischemic heart disease	55,067	79.1%	55,153	79.2%	-0.123	-0.003
Renal disorders	27,364	39.3%	27,495	39.5%	-0.188	-0.004
Serious allergies	8,047	11.6%	8,038	11.5%	0.013	0.000

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Table 1b. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

	Medical Product			Covariate Balance		
	S	v	ACEI			
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	28,444	40.8%	28,475	40.9%	-0.045	-0.001
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	60,338	86.6%	60,422	86.8%	-0.121	-0.004
Everolimus	11	0.0%	12	0.0%	-0.001	-0.001
Nonsteroidal anti-inflammatory drugs (NSAIDs)	7,793	11.2%	7,766	11.2%	0.039	0.001
Sirolimus	****	****	14	0.0%	-0.009	-0.007
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.9	13.7	17.9	20.5	-0.041	-0.002
Mean number of emergency room encounters	0.7	1.4	0.7	1.2	-0.003	-0.002
Mean number of inpatient hospital encounters	0.8	1.1	0.8	0.9	-0.011	-0.010
Mean number of non-acute institutional encounters	0.2	0.8	0.2	0.7	-0.006	-0.008
Mean number of other ambulatory encounters	8.1	12.2	8.2	11.0	-0.062	-0.005
Mean number of filled prescriptions	31.3	19.8	28.2	22.9	3.118	0.146
Mean number of generics	13.1	5.1	12.2	5.7	0.922	0.170
Mean number of unique drug classes	11.4	4.5	11.4	5.0	-0.041	-0.009

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requesterdefined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity sc ore predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1c. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,

	Medical Product			Covariate Balance		
	SV ACEI		CEI			
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Patients (Number)	69,639	100.0%	694,882	100.0%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.1	11.4	72.6	12.5	-0.466	-0.039
Age	Number	Percent	Number	Percent		
18-44 years	1,968	2.8%	21,875	3.1%	-0.321	-0.019
45-54 years	4,182	6.0%	45,805	6.6%	-0.587	-0.025
55-64 years	9,832	14.1%	98,637	14.2%	-0.076	-0.002
65+ years	53,657	77.0%	528,564	76.1%	0.984	0.025
Sex						
Female	33,257	47.8%	330,693	47.6%	0.167	0.003
Male	36,382	52.2%	364,189	52.4%	-0.167	-0.003
Race						
American Indian or Alaska Native	396	0.6%	4,349	0.6%	-0.057	-0.007
Asian	724	1.0%	7,777	1.1%	-0.079	-0.008
Black or African American	8,622	12.4%	92,009	13.2%	-0.860	-0.026
Native Hawaiian or Other Pacific Islander	58	0.1%	732	0.1%	-0.023	-0.007
Unknown	11,379	16.3%	99,758	14.4%	1.984	0.092
White	48,459	69.6%	490,256	70.6%	-0.966	-0.025
Hispanic Origin	1,327	1.9%	15,544	2.2%	-0.332	-0.023
Year						
2015	7,015	10.1%	80,407	11.6%	-1.498	-0.048
2016	15,676	22.5%	166,839	24.0%	-1.499	-0.035
2017	15,798	22.7%	158,018	22.7%	-0.055	-0.001
2018	15,486	22.2%	147,402	21.2%	1.025	0.025
2019	15,371	22.1%	140,377	20.2%	1.871	0.046
2020	293	3.2%	1,839	2.5%	0.682	0.041
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.9	3.2	5.8	3.0	0.115	0.037
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	33,199	47.7%	322,089	46.4%	1.321	0.027
Angioedema (-183, -1)	76	0.1%	860	0.1%	-0.015	-0.004
Angioedema (ever, -1)	501	0.7%	7,303	1.1%	-0.331	-0.035
Diabetes	32,924	47.3%	328,219	47.2%	0.045	0.001
Ischemic heart disease	45,178	64.9%	443,528	63.8%	1.046	0.022
Renal disorders	29,955	43.0%	288,849	41.6%	1.446	0.029
Serious allergies	11,113	16.0%	108,563	15.6%	0.334	0.009

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Table 1c. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,

		Medical	Covariate Balance			
	S	V	A	CEI		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	25,967	37.3%	255,647	36.8%	0.497	0.010
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	48,928	70.3%	471,272	67.8%	2.439	0.053
Everolimus	33	0.0%	177	0.0%	0.022	0.011
Nonsteroidal anti-inflammatory drugs (NSAIDs)	8,966	12.9%	88,045	12.7%	0.204	0.006
Sirolimus	21	0.0%	195	0.0%	0.001	0.001
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	18.0	14.6	17.4	19.8	0.600	0.035
Mean number of emergency room encounters	1.0	3.4	0.8	1.7	0.152	0.056
Mean number of inpatient hospital encounters	1.1	1.5	1.0	1.1	0.091	0.067
Mean number of non-acute institutional encounters	0.5	1.3	0.4	1.0	0.063	0.055
Mean number of other ambulatory encounters	13.1	20.5	12.4	17.6	0.699	0.037
Mean number of filled prescriptions	30.6	20.9	27.0	23.0	3.589	0.164
Mean number of generics	12.8	5.5	11.6	5.7	1.224	0.218
Mean number of unique drug classes	11.1	4.8	10.8	5.0	0.239	0.049

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1d. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical	Covariate Balance			
	S	SV	AF	RBs		
Characteristic ^{1,2}	Newskan	D	Name Is an	B	Absolute	Standardized
Patients (Number)	Number 49,140	Percent 100.0%	Number 337,083	Percent 100.0%	Difference -	Difference -
rations (Namber)	43,140	Standard	337,003	Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.6	10.7	73.8	12.0	-1.241	-0.109
Age	Number	Percent	Number	Percent		
18-44 years	1,164	2.4%	8,502	2.5%	-0.153	-0.010
45-54 years	2,653	5.4%	18,293	5.4%	-0.028	-0.001
55-64 years	5,990	12.2%	40,547	12.0%	0.161	0.005
65+ years	39,333	80.0%	269,741	80.0%	0.021	0.001
Sex						
Female	19,226	39.1%	187,871	55.7%	-16.609	-0.337
Male	29,914	60.9%	149,212	44.3%	16.609	0.337
Race						
American Indian or Alaska Native	133	0.3%	1,948	0.6%	-0.307	-0.047
Asian	1,070	2.2%	7,811	2.3%	-0.140	-0.009
Black or African American	6,989	14.2%	55,801	16.6%	-2.331	-0.065
Native Hawaiian or Other Pacific Islander	61	0.1%	478	0.1%	-0.018	-0.005
Unknown	8,082	16.4%	47,793	14.2%	2.268	0.063
White	32,805	66.8%	223,252	66.2%	0.528	0.011
Hispanic Origin	1,135	2.3%	9,032	2.7%	-0.370	-0.024
Year						
2015	878	1.8%	32,231	9.6%	-7.775	-0.341
2016	6,685	13.6%	70,696	21.0%	-7.369	-0.196
2017	11,072	22.5%	73,800	21.9%	0.638	0.015
2018	13,611	27.7%	81,657	24.2%	3.474	0.079
2019	16,598	33.8%	77,594	23.0%	10.758	0.240
2020	296	4.9%	1,105	3.2%	1.652	0.084
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.4	2.7	5.8	3.0	-0.374	-0.133
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	26,106	53.1%	169,522	50.3%	2.835	0.057
Angioedema (-183, -1)	58	0.1%	825	0.2%	-0.127	-0.030
Angioedema (ever, -1)	750	1.5%	7,357	2.2%	-0.656	-0.049
Diabetes	26,110	53.1%	173,497	51.5%	1.664	0.033
Ischemic heart disease	38,297	77.9%	203,944	60.5%	17.432	0.385
Renal disorders	21,237	43.2%	154,620	45.9%	-2.653	-0.053
Serious allergies	6,466	13.2%	54,435	16.1%	-2.991	-0.085

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Table 1d. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical	Covariate Balance			
	S	V	AF	RBs		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	21,703	44.2%	134,451	39.9%	4.279	0.087
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	42,889	87.3%	222,859	66.1%	21.165	0.517
Everolimus	15	0.0%	98	0.0%	0.001	0.001
Nonsteroidal anti-inflammatory drugs (NSAIDs)	5,633	11.5%	44,187	13.1%	-1.645	-0.050
Sirolimus	****	****	142	0.0%	-0.030	-0.018
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	19.2	14.8	20.4	22.5	-1.228	-0.064
Mean number of emergency room encounters	0.6	1.3	0.8	1.7	-0.169	-0.112
Mean number of inpatient hospital encounters	0.8	1.1	0.8	1.1	-0.079	-0.071
Mean number of non-acute institutional encounters	0.2	0.7	0.4	1.0	-0.174	-0.192
Mean number of other ambulatory encounters	8.1	11.6	11.7	17.4	-3.639	-0.246
Mean number of filled prescriptions	32.5	20.9	27.8	22.3	4.697	0.217
Mean number of generics	13.8	5.4	12.0	5.8	1.857	0.331
Mean number of unique drug classes	12.0	4.7	11.2	5.1	0.812	0.164

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity scor e predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1e. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
	S	SV .	AF	RBs		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Patients (Number)	49,137	100.0%	49,137	14.6%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.6	10.7	72.6	11.5	-0.016	-0.001
Age	Number	Percent	Number	Percent		
18-44 years	1,164	2.4%	1,231	2.5%	-0.136	-0.009
45-54 years	2,652	5.4%	2,977	6.1%	-0.661	-0.029
55-64 years	5,988	12.2%	6,682	13.6%	-1.412	-0.043
65+ years	39,333	80.0%	38,247	77.8%	2.210	0.058
Sex						
Female	19,226	39.1%	19,287	39.3%	-0.124	-0.003
Male	29,911	60.9%	29,850	60.7%	0.124	0.003
Race						
American Indian or Alaska Native	133	0.3%	144	0.3%	-0.022	-0.004
Asian	1,070	2.2%	1,059	2.2%	0.022	0.002
Black or African American	6,988	14.2%	7,004	14.3%	-0.033	-0.001
Native Hawaiian or Other Pacific Islander	61	0.1%	53	0.1%	0.016	0.005
Unknown	8,080	16.4%	8,091	16.5%	-0.022	-0.001
White	32,805	66.8%	32,786	66.7%	0.039	0.001
Hispanic Origin	1,135	2.3%	1,221	2.5%	-0.175	-0.011
Year						
2015	878	1.8%	822	1.7%	0.114	0.009
2016	6,685	13.6%	6,735	13.7%	-0.102	-0.003
2017	11,072	22.5%	11,079	22.5%	-0.014	-0.000
2018	13,611	27.7%	13,558	27.6%	0.108	0.002
2019	16,595	33.8%	16,643	33.9%	-0.098	-0.002
2020	296	4.9%	300	5.0%	-0.066	-0.003
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.4	2.7	5.4	2.7	0.001	0.000
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	26,103	53.1%	26,126	53.2%	-0.047	-0.001
Angioedema (-183, -1)	58	0.1%	56	0.1%	0.004	0.001
Angioedema (ever, -1)	750	1.5%	1,084	2.2%	-0.680	-0.050
Diabetes	26,109	53.1%	25,978	52.9%	0.267	0.005
Ischemic heart disease	38,294	77.9%	38,161	77.7%	0.271	0.007
Renal disorders	21,235	43.2%	21,281	43.3%	-0.094	-0.002
Serious allergies	6,466	13.2%	6,500	13.2%	-0.069	-0.002

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Table 1e. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
	sv		AF	RBs		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	21,700	44.2%	21,734	44.2%	-0.069	-0.001
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	42,886	87.3%	42,937	87.4%	-0.104	-0.003
Everolimus	15	0.0%	19	0.0%	-0.008	-0.004
Nonsteroidal anti-inflammatory drugs (NSAIDs)	5,633	11.5%	5,752	11.7%	-0.242	-0.008
Sirolimus	****	****	****	****	0.004	0.004
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	19.2	14.8	19.2	19.8	-0.002	-0.000
Mean number of emergency room encounters	0.6	1.3	0.6	1.2	-0.010	-0.008
Mean number of inpatient hospital encounters	0.8	1.1	0.8	1.0	0.000	0.000
Mean number of non-acute institutional encounters	0.2	0.7	0.2	0.7	-0.002	-0.002
Mean number of other ambulatory encounters	8.1	11.6	8.1	11.0	0.006	0.001
Mean number of filled prescriptions	32.5	20.9	29.7	22.4	2.717	0.125
Mean number of generics	13.8	5.4	12.9	5.8	0.967	0.173
Mean number of unique drug classes	12.0	4.7	12.0	5.1	-0.034	-0.007

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Covariate Balance

Table 1f. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,

Medical Product

		ivieuicai	Product		COvariate Balance	
	9	SV I	Al	RBs	Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	49,140	100.0%	337,083	100.0%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	73.6	11.1	73.7	12.0	-0.109	-0.009
Age	Number	Percent	Number	Percent		
18-44 years	1,100	2.2%	8,414	2.5%	-0.258	-0.017
45-54 years	2,349	4.8%	18,410	5.5%	-0.682	-0.031
55-64 years	5,573	11.3%	40,943	12.1%	-0.806	-0.026
65+ years	40,119	81.6%	269,315	79.9%	1.746	0.047
Sex						
Female	26,639	54.2%	181,198	53.8%	0.456	0.009
Male	22,501	45.8%	155,885	46.2%	-0.456	-0.009
Race						
American Indian or Alaska Native	297	0.6%	1,825	0.5%	0.063	0.008
Asian	1,046	2.1%	7,748	2.3%	-0.170	-0.012
Black or African American	7,384	15.0%	55,001	16.3%	-1.289	-0.036
Native Hawaiian or Other Pacific Islander	66	0.1%	475	0.1%	-0.007	-0.002
Unknown	7,753	15.8%	47,835	14.2%	1.587	0.069
White	32,593	66.3%	224,199	66.5%	-0.184	-0.004
Hispanic Origin	1,061	2.2%	8,949	2.7%	-0.495	-0.032
Year						
2015	3,730	7.6%	28,917	8.6%	-0.988	-0.036
2016	9,534	19.4%	67,607	20.1%	-0.655	-0.016
2017	10,600	21.6%	74,244	22.0%	-0.455	-0.011
2018	12,309	25.0%	83,326	24.7%	0.329	0.008
2019	12,738	25.9%	81,807	24.3%	1.653	0.038
2020	230	3.8%	1,181	3.5%	0.331	0.018
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.7	3.0	5.7	2.9	-0.003	-0.001
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	25,269	51.4%	170,719	50.6%	0.777	0.016
Angioedema (-183, -1)	115	0.2%	770	0.2%	0.006	0.001
Angioedema (ever, -1)	775	1.6%	7,342	2.2%	-0.601	-0.044
Diabetes	24,847	50.6%	174,248	51.7%	-1.128	-0.023
Ischemic heart disease	31,038	63.2%	211,390	62.7%	0.451	0.009
Renal disorders	22,193	45.2%	153,842	45.6%	-0.477	-0.010
Serious allergies	7,717	15.7%	53,278	15.8%	-0.101	-0.003

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Table 1f. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,

		Medical	Covariate Balance			
	sv		ARBs			
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	20,111	40.9%	136,253	40.4%	0.505	0.010
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	34,636	70.5%	231,958	68.8%	1.671	0.036
Everolimus	14	0.0%	98	0.0%	-0.000	-0.000
Nonsteroidal anti-inflammatory drugs (NSAIDs)	6,349	12.9%	43,543	12.9%	0.003	0.000
Sirolimus	15	0.0%	129	0.0%	-0.007	-0.004
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	19.9	17.4	20.3	22.2	-0.439	-0.022
Mean number of emergency room encounters	0.8	2.7	0.8	1.6	0.063	0.028
Mean number of inpatient hospital encounters	0.8	1.2	0.8	1.1	0.007	0.006
Mean number of non-acute institutional encounters	0.4	1.1	0.4	1.0	0.008	0.008
Mean number of other ambulatory encounters	11.3	18.2	11.3	16.8	0.017	0.001
Mean number of filled prescriptions	31.2	22.2	28.0	22.3	3.224	0.145
Mean number of generics	13.2	5.5	12.1	5.8	1.146	0.202
Mean number of unique drug classes	11.5	4.8	11.3	5.1	0.153	0.031

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity scor e predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1g. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical	Covariate Balance			
	S	V	A	CEI		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Patients (Number)	49,629	100.0%	695,068	100.0%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	70.4	11.1	72.7	12.5	-2.309	-0.196
Age	Number	Percent	Number	Percent		
18-44 years	1,592	3.2%	21,593	3.1%	0.101	0.006
45-54 years	3,425	6.9%	45,072	6.5%	0.417	0.017
55-64 years	8,067	16.3%	97,279	14.0%	2.259	0.063
65+ years	36,545	73.6%	531,124	76.4%	-2.777	-0.064
Sex						
Female	14,886	30.0%	341,922	49.2%	-19.198	-0.400
Male	34,743	70.0%	353,146	50.8%	19.198	0.400
Race						
American Indian or Alaska Native	165	0.3%	4,526	0.7%	-0.319	-0.046
Asian	526	1.1%	7,873	1.1%	-0.073	-0.007
Black or African American	6,074	12.2%	92,135	13.3%	-1.017	-0.030
Native Hawaiian or Other Pacific Islander	46	0.1%	741	0.1%	-0.014	-0.004
Unknown	8,192	16.5%	99,667	14.3%	2.167	0.060
White	34,626	69.8%	490,126	70.5%	-0.745	-0.016
Hispanic Origin	990	2.0%	15,590	2.2%	-0.248	-0.017
Year						
2015	951	1.9%	87,092	12.5%	-10.614	-0.419
2016	6,862	13.8%	172,883	24.9%	-11.046	-0.282
2017	11,714	23.6%	156,612	22.5%	1.071	0.025
2018	13,939	28.1%	143,032	20.6%	7.508	0.176
2019	15,918	32.1%	133,697	19.2%	12.839	0.297
2020	245	3.9%	1,752	2.4%	1.500	0.086
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.1	2.6	5.8	3.0	-0.734	-0.262
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	23,931	48.2%	320,785	46.2%	2.068	0.041
Angioedema (-183, -1)	46	0.1%	864	0.1%	-0.032	-0.010
Angioedema (ever, -1)	333	0.7%	7,320	1.1%	-0.382	-0.041
Diabetes	24,859	50.1%	326,119	46.9%	3.171	0.063
Ischemic heart disease	39,138	78.9%	433,124	62.3%	16.547	0.369
Renal disorders	18,823	37.9%	289,848	41.7%	-3.773	-0.077
Serious allergies	5,370	10.8%	110,996	16.0%	-5.149	-0.152

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Table 1g. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical	Covariate Balance			
	sv		A	CEI		
Ch					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent 41.0%	Number	Percent 36.4%	Difference 4.620	0.095
Ambulatory allergies or treatment and not serious allergies	20,361	41.0%	253,046	30.4%	4.620	0.095
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	42,882	86.4%	458,271	65.9%	20.473	0.495
Everolimus	11	0.0%	183	0.0%	-0.004	-0.003
Nonsteroidal anti-inflammatory drugs (NSAIDs)	5,678	11.4%	88,974	12.8%	-1.360	-0.042
Sirolimus	****	****	208	0.0%	-0.018	-0.012
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.5	13.4	17.4	19.7	0.193	0.011
Mean number of emergency room encounters	0.6	1.3	0.9	1.8	-0.233	-0.149
Mean number of inpatient hospital encounters	0.7	1.0	1.0	1.2	-0.280	-0.256
Mean number of non-acute institutional encounters	0.2	0.7	0.4	1.1	-0.258	-0.289
Mean number of other ambulatory encounters	7.3	10.6	12.8	18.0	-5.565	-0.377
Mean number of filled prescriptions	31.8	20.3	26.9	23.0	4.963	0.229
Mean number of generics	13.2	5.1	11.5	5.7	1.669	0.309
Mean number of unique drug classes	11.4	4.5	10.8	5.0	0.623	0.131

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1h. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedemain the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
	S	SV .	A	CEI		
21 12		_		_	Absolute	Standardized
Characteristic ^{1,2} Patients (Number)	Number 49,628	Percent	Number 49,628	Percent 7.1%	Difference -	Difference
Patients (Number)	49,028	100.0%	49,028		•	-
Danie a marchina	20	Standard		Standard		
Demographics Mean age (years)	Mean 70.4	Deviation 11.1	Mean 70.5	Deviation 12.0	-0.018	-0.002
Age					-0.018	-0.002
18-44 years	Number 1,592	Percent 3.2%	Number 1,778	Percent 3.6%	-0.375	-0.021
45-54 years	3,425	6.9%	3,879	7.8%	-0.915	-0.021
55-64 years	8,066	16.3%	8,362	16.8%	-0.515	-0.036
65+ years	36,545	73.6%	35,609	71.8%	1.886	0.045
Sex	30,343	73.070	33,003	71.070	1.000	0.043
Female	14,886	30.0%	15,194	30.6%	-0.621	-0.014
Male	34,742	70.0%	34,434	69.4%	0.621	0.014
Race	34,742	70.076	34,434	05.470	0.021	0.014
American Indian or Alaska Native	165	0.3%	157	0.3%	0.016	0.003
Asian	526	1.1%	498	1.0%	0.016	0.003
Black or African American	6,073	1.1%	6,128	1.0%	-0.111	-0.003
Native Hawaiian or Other Pacific Islander	46	0.1%	60	0.1%	-0.111	-0.003
Unknown	8,192	16.5%	8,156	16.4%	0.073	0.003
White	34,626	69.8%	34,629	69.8%	-0.006	-0.000
Hispanic Origin	990	2.0%	1,109	2.2%	-0.240	-0.017
Year	054	4.00/	005	4.00/	0.442	0.000
2015	951	1.9%	895	1.8%	0.113	0.008
2016	6,862	13.8%	6,855	13.8%	0.014	0.000
2017	11,714	23.6%	11,709	23.6%	0.010	0.000
2018	13,939	28.1%	14,045	28.3%	-0.214	-0.005
2019	15,917	32.1%	15,886	32.0%	0.062	0.001
2020	245	3.9%	238	3.8%	0.112	0.006
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation	2.222	0.000
Charlson/Elixhauser Combined Comorbidity	5.1	2.6	5.1	2.6	-0.008	-0.003
Score ³						
	Number	Percent	Number	Percent	2.225	2.221
Ambulatory allergies or allergy treatment	23,930	48.2%	23,912	48.2%	0.036	0.001
Angioedema (-183, -1)	46	0.1%	54	0.1%	-0.016	-0.005
Angioedema (ever, -1)	333	0.7%	539	1.1%	-0.415	-0.044
Diabetes	24,858	50.1%	24,757	49.9%	0.204	0.004
Ischemic heart disease	39,137	78.9%	39,128	78.8%	0.018	0.000
Renal disorders	18,823	37.9%	18,881	38.0%	-0.117	-0.002
Serious allergies	5,370	10.8%	5,418	10.9%	-0.097	-0.003

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Table 1h. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedemain the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
	S	V	A	CEI		
21 1.2					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Ambulatory allergies or treatment and not serious allergies	20,360	41.0%	20,491	41.3%	-0.264	-0.005
History of Use:	42,881	86.4%	43,054	86.8%	-0.349	-0.010
Diuretics (thiazides, potassium sparing, loop diuretics)	42,881	80.4%	43,054	80.8%	-0.349	-0.010
Everolimus	11	0.0%	14	0.0%	-0.006	-0.004
Nonsteroidal anti-inflammatory drugs	5,678	11.4%	5,746	11.6%	-0.137	-0.004
(NSAIDs)						
Sirolimus	****	****	****	****	-0.002	-0.002
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.5	13.4	17.6	20.0	-0.048	-0.003
Mean number of emergency room encounters	0.6	1.3	0.6	1.1	-0.007	-0.006
Mean number of inpatient hospital	0.7	1.0	0.7	0.9	-0.004	-0.004
encounters						
Mean number of non-acute institutional encounters	0.2	0.7	0.2	0.7	-0.003	-0.005
Mean number of other ambulatory	7.3	10.6	7.3	9.7	-0.004	-0.000
encounters						
Mean number of filled prescriptions	31.8	20.3	28.0	22.5	3.788	0.177
Mean number of generics	13.2	5.1	12.2	5.6	1.029	0.192
Mean number of unique drug classes	11.4	4.5	11.4	5.0	-0.002	-0.000

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Covariate Balance

Table 1i. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

Medical Product

	iviedicai Product			Covariate Balance		
	S	SV	Al	RBs	Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	35,703	100.0%	337,204	100.0%	-	-
	,	Standard	,	Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.8	10.6	73.8	12.0	-1.042	-0.092
Age	Number	Percent	Number	Percent		
18-44 years	774	2.2%	8,505	2.5%	-0.354	-0.023
45-54 years	1,794	5.0%	18,304	5.4%	-0.403	-0.018
55-64 years	4,275	12.0%	40,567	12.0%	-0.057	-0.002
65+ years	28,860	80.8%	269,828	80.0%	0.814	0.021
Sex						
Female	13,901	38.9%	187,925	55.7%	-16.795	-0.341
Male	21,802	61.1%	149,279	44.3%	16.795	0.341
Race						
American Indian or Alaska Native	86	0.2%	1,948	0.6%	-0.337	-0.053
Asian	863	2.4%	7,814	2.3%	0.100	0.007
Black or African American	4,832	13.5%	55,825	16.6%	-3.021	-0.085
Native Hawaiian or Other Pacific Islander	46	0.1%	478	0.1%	-0.013	-0.004
Unknown	5,777	16.2%	47,811	14.2%	2.002	0.056
White	24,099	67.5%	223,328	66.2%	1.269	0.027
Hispanic Origin	887	2.5%	9,034	2.7%	-0.195	-0.012
Year						
2015	615	1.7%	32,231	9.6%	-7.836	-0.345
2016	4,471	12.5%	70,701	21.0%	-8.444	-0.228
2017	7,825	21.9%	73,818	21.9%	0.026	0.001
2018	10,142	28.4%	81,689	24.2%	4.181	0.095
2019	12,431	34.8%	77,659	23.0%	11.788	0.262
2020	219	5.2%	1,106	3.2%	2.000	0.099
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.3	2.6	5.8	3.0	-0.460	-0.165
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	19,158	53.7%	169,574	50.3%	3.371	0.068
Angioedema (-183, -1)	35	0.1%	825	0.2%	-0.147	-0.035
Angioedema (ever, -1)	541	1.5%	7,359	2.2%	-0.667	-0.050
Diabetes	19,018	53.3%	173,568	51.5%	1.795	0.036
Ischemic heart disease	27,797	77.9%	204,033	60.5%	17.349	0.383
Renal disorders	14,977	41.9%	154,691	45.9%	-3.926	-0.079
Serious allergies	4,472	12.5%	54,454	16.1%	-3.623	-0.104

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Table 1i. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical	Covariate Balance			
	g	SV	AF	RBs		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	16,113	45.1%	134,493	39.9%	5.246	0.106
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	31,138	87.2%	222,966	66.1%	21.092	0.515
Everolimus	****	****	98	0.0%	-0.001	-0.001
Nonsteroidal anti-inflammatory drugs (NSAIDs)	4,177	11.7%	44,193	13.1%	-1.406	-0.043
Sirolimus	****	****	142	0.0%	-0.028	-0.017
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	19.0	14.7	20.4	22.5	-1.447	-0.076
Mean number of emergency room encounters	0.6	1.3	8.0	1.7	-0.200	-0.134
Mean number of inpatient hospital encounters	0.7	1.0	0.8	1.1	-0.130	-0.120
Mean number of non-acute institutional encounters	0.2	0.7	0.4	1.0	-0.211	-0.241
Mean number of other ambulatory encounters	7.4	10.4	11.7	17.4	-4.289	-0.299
Mean number of filled prescriptions	33.3	21.7	27.8	22.3	5.583	0.254
Mean number of generics	14.0	5.4	12.0	5.8	2.009	0.358
Mean number of unique drug classes	12.1	4.8	11.2	5.1	0.886	0.179

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

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Table 1j. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
		SV ARBs				
			A		Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	35,702	100.0%	35,702	10.6%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.8	10.6	72.8	11.4	-0.050	-0.005
Age	Number	Percent	Number	Percent		
18-44 years	774	2.2%	796	2.2%	-0.062	-0.004
45-54 years	1,794	5.0%	2,104	5.9%	-0.868	-0.039
55-64 years	4,275	12.0%	4,789	13.4%	-1.440	-0.045
65+ years	28,859	80.8%	28,013	78.5%	2.370	0.063
Sex						
Female	13,901	38.9%	14,074	39.4%	-0.485	-0.010
Male	21,801	61.1%	21,628	60.6%	0.485	0.010
Race						
American Indian or Alaska Native	86	0.2%	85	0.2%	0.003	0.001
Asian	862	2.4%	886	2.5%	-0.067	-0.004
Black or African American	4,832	13.5%	4,869	13.6%	-0.104	-0.003
Native Hawaiian or Other Pacific Islander	46	0.1%	43	0.1%	0.008	0.002
Unknown	5,777	16.2%	5,754	16.1%	0.064	0.003
White	24,099	67.5%	24,065	67.4%	0.095	0.002
Hispanic Origin	887	2.5%	899	2.5%	-0.034	-0.002
Year						
2015	615	1.7%	586	1.6%	0.081	0.006
2016	4,471	12.5%	4,444	12.4%	0.076	0.002
2017	7,824	21.9%	7,801	21.9%	0.064	0.002
2018	10,142	28.4%	10,242	28.7%	-0.280	-0.006
2019	12,431	34.8%	12,429	34.8%	0.006	0.000
2020	219	5.2%	200	4.8%	0.455	0.021
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.3	2.6	5.3	2.6	0.016	0.006
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	19,157	53.7%	18,976	53.2%	0.507	0.010
Angioedema (-183, -1)	35	0.1%	38	0.1%	-0.008	-0.003
Angioedema (ever, -1)	541	1.5%	731	2.0%	-0.532	-0.040
Diabetes	19,017	53.3%	19,134	53.6%	-0.328	-0.007
Ischemic heart disease	27,796	77.9%	27,790	77.8%	0.017	0.000
Renal disorders	14,977	42.0%	14,929	41.8%	0.134	0.003
Serious allergies	4,472	12.5%	4,463	12.5%	0.025	0.001
-						

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Table 1j. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

	Medical Product				Covariate Balance	
	sv		ARBs			
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference
Ambulatory allergies or treatment and not serious allergies	16,112	45.1%	16,023	44.9%	0.249	0.005
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	31,137	87.2%	31,197	87.4%	-0.168	-0.005
Everolimus	****	****	****	****	0.003	0.002
Nonsteroidal anti-inflammatory drugs (NSAIDs)	4,177	11.7%	4,171	11.7%	0.017	0.001
Sirolimus	****	****	****	****	-0.008	-0.006
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	19.0	14.7	18.8	19.1	0.195	0.011
Mean number of emergency room encounters	0.6	1.3	0.6	1.1	-0.008	-0.007
Mean number of inpatient hospital encounters	0.7	1.0	0.7	1.0	0.003	0.003
Mean number of non-acute institutional encounters	0.2	0.7	0.2	0.7	-0.002	-0.003
Mean number of other ambulatory encounters	7.4	10.4	7.4	10.0	0.032	0.003
Mean number of filled prescriptions	33.3	21.7	30.0	22.9	3.305	0.148
Mean number of generics	14.0	5.4	12.9	5.8	1.078	0.192
Mean number of unique drug classes	12.1	4.7	12.1	5.1	-0.007	-0.001

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requesterdefined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity scor e predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1k. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical	Covariate Balance			
	S	SV ACEI				
Character 1,2					Absolute	Standardized
Patients (Number)	Number 69,639	Percent 100.0%	Number 694,882	100.0%	Difference	Difference -
ratients (Number)	09,039		034,002		-	-
Demographics	Mean	Standard Deviation	Mean	Standard Deviation		
Mean age (years)	70.2	11.2	72.7	12.5	-2.563	-0.216
Age	Number	Percent	Number	Percent	2.303	0.210
18-44 years	2,412	3.5%	21,587	3.1%	0.357	0.020
45-54 years	5,115	7.3%	45,057	6.5%	0.861	0.034
55-64 years	11,494	16.5%	97,244	14.0%	2.511	0.070
65+ years	50,618	72.7%	530,994	76.4%	-3.729	-0.086
Sex	,	. =,				
Female	21,199	30.4%	341,867	49.2%	-18.757	-0.390
Male	48,440	69.6%	353,015	50.8%	18.757	0.390
Race	,		,			
American Indian or Alaska Native	242	0.3%	4,525	0.7%	-0.304	-0.043
Asian	666	1.0%	, 7,871	1.1%	-0.176	-0.017
Black or African American	9,015	12.9%	92,098	13.3%	-0.308	-0.009
Native Hawaiian or Other Pacific Islander	66	0.1%	741	0.1%	-0.012	-0.004
Unknown	11,656	16.7%	99,645	14.3%	2.398	0.066
White	47,994	68.9%	490,002	70.5%	-1.598	-0.035
Hispanic Origin	1,351	1.9%	15,586	2.2%	-0.303	-0.021
Year						
2015	1,349	1.9%	87,092	12.5%	-10.596	-0.418
2016	10,510	15.1%	172,880	24.9%	-9.787	-0.247
2017	16,864	24.2%	156,573	22.5%	1.684	0.040
2018	19,077	27.4%	142,979	20.6%	6.818	0.160
2019	21,511	30.9%	133,608	19.2%	11.662	0.272
2020	328	3.6%	1,750	2.4%	1.194	0.070
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.2	2.7	5.8	3.0	-0.610	-0.214
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	33,754	48.5%	320,699	46.2%	2.318	0.046
Angioedema (-183, -1)	83	0.1%	864	0.1%	-0.005	-0.001
Angioedema (ever, -1)	494	0.7%	7,317	1.1%	-0.344	-0.037
Diabetes	35,071	50.4%	326,005	46.9%	3.446	0.069
Ischemic heart disease	55,067	79.1%	432,968	62.3%	16.767	0.375
Renal disorders	27,364	39.3%	289,746	41.7%	-2.403	-0.049
Serious allergies	8,047	11.6%	110,960	16.0%	-4.413	-0.128

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Table 1k. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

	Medical Product				Covariate Balance	
	S	٧	A	CEI		
-1 12		_		_	Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Ambulatory allergies or treatment and not serious allergies	28,444	40.8%	252,983	36.4%	4.438	0.091
History of Use:						
Diuretics (thiazides, potassium sparing, loop diuretics)	60,338	86.6%	458,102	65.9%	20.719	0.502
Everolimus	11	0.0%	183	0.0%	-0.011	-0.007
Nonsteroidal anti-inflammatory drugs (NSAIDs)	7,793	11.2%	88,957	12.8%	-1.611	-0.050
Sirolimus	****	****	208	0.0%	-0.018	-0.013
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.9	13.7	17.4	19.7	0.531	0.031
Mean number of emergency room encounters	0.7	1.4	0.9	1.8	-0.188	-0.115
Mean number of inpatient hospital encounters	0.8	1.1	1.0	1.2	-0.211	-0.186
Mean number of non-acute institutional encounters	0.2	0.8	0.4	1.1	-0.217	-0.235
Mean number of other ambulatory encounters	8.1	12.2	12.8	18.0	-4.732	-0.308
Mean number of filled prescriptions	31.3	19.8	26.9	23.0	4.408	0.205
Mean number of generics	13.1	5.1	11.5	5.7	1.614	0.297
Mean number of unique drug classes	11.4	4.5	10.8	5.0	0.626	0.131

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1l. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical		Covariate Balance		
	S	V	A	CEI		
21 1.2					Absolute	Standardized
Characteristic ^{1,2} Patients (Number)	Number 69,639	Percent 100.0%	Number 69,639	Percent 10.0%	Difference	Difference
ratients (Number)	09,039		09,039		-	-
Demographics	Mean	Standard Deviation	Mean	Standard Deviation		
Mean age (years)	70.2	11.2	70.2	12.2	-0.019	-0.002
Age	Number	Percent	Number	Percent		
18-44 years	2,412	3.5%	2,717	3.9%	-0.438	-0.024
45-54 years	5,115	7.3%	5,694	8.2%	-0.831	-0.032
55-64 years	11,494	16.5%	11,900	17.1%	-0.583	-0.016
65+ years	50,618	72.7%	49,328	70.8%	1.852	0.044
Sex						
Female	21,199	30.4%	21,398	30.7%	-0.286	-0.006
Male	48,440	69.6%	48,241	69.3%	0.286	0.006
Race						
American Indian or Alaska Native	242	0.3%	242	0.3%	0.000	0.000
Asian	666	1.0%	662	1.0%	0.006	0.001
Black or African American	9,015	12.9%	9,043	13.0%	-0.040	-0.001
Native Hawaiian or Other Pacific Islander	66	0.1%	75	0.1%	-0.013	-0.004
Unknown	11,656	16.7%	11,662	16.7%	-0.009	-0.000
White	47,994	68.9%	47,955	68.9%	0.056	0.001
Hispanic Origin	1,351	1.9%	1,521	2.2%	-0.244	-0.017
Year						
2015	1,349	1.9%	1,255	1.8%	0.135	0.010
2016	10,510	15.1%	10,469	15.0%	0.059	0.002
2017	16,864	24.2%	16,928	24.3%	-0.092	-0.002
2018	19,077	27.4%	19,069	27.4%	0.011	0.000
2019	21,511	30.9%	21,555	31.0%	-0.063	-0.001
2020	328	3.6%	363	4.0%	-0.385	-0.020
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.2	2.7	5.2	2.6	-0.017	-0.006
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	33,754	48.5%	33,596	48.2%	0.227	0.005
Angioedema (-183, -1)	83	0.1%	92	0.1%	-0.013	-0.004
Angioedema (ever, -1)	494	0.7%	723	1.0%	-0.329	-0.035
Diabetes	35,071	50.4%	34,906	50.1%	0.237	0.005
Ischemic heart disease	55,067	79.1%	55,153	79.2%	-0.123	-0.003
Renal disorders	27,364	39.3%	27,495	39.5%	-0.188	-0.004
Serious allergies	8,047	11.6%	8,038	11.5%	0.013	0.000

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Table 1I. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical		Covariate Balance			
	S	V	A	CEI			
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference	
Ambulatory allergies or treatment and not serious allergies	28,444	40.8%	28,475	40.9%	-0.045	-0.001	
History of Use:							
Diuretics (thiazides, potassium sparing, loop diuretics)	60,338	86.6%	60,422	86.8%	-0.121	-0.004	
Everolimus	11	0.0%	12	0.0%	-0.001	-0.001	
Nonsteroidal anti-inflammatory drugs (NSAIDs)	7,793	11.2%	7,766	11.2%	0.039	0.001	
Sirolimus	****	****	14	0.0%	-0.009	-0.007	
		Standard		Standard			
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation			
Mean number of ambulatory encounters	17.9	13.7	17.9	20.5	-0.041	-0.002	
Mean number of emergency room encounters	0.7	1.4	0.7	1.2	-0.003	-0.002	
Mean number of inpatient hospital encounters	0.8	1.1	0.8	0.9	-0.011	-0.010	
Mean number of non-acute institutional encounters	0.2	0.8	0.2	0.7	-0.006	-0.008	
Mean number of other ambulatory encounters	8.1	12.2	8.2	11.0	-0.062	-0.005	
Mean number of filled prescriptions	31.3	19.8	28.2	22.9	3.118	0.146	
Mean number of generics	13.1	5.1	12.2	5.7	0.922	0.170	
Mean number of unique drug classes	11.4	4.5	11.4	5.0	-0.041	-0.009	

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity scor e predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 1m. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical		Covaria	te Balance	
	9	SV	А	CEI		
12					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	49,140	100.0%	337,083	100.0%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation	1 241	0.100
Mean age (years)	72.6	10.7	73.8	12.0	-1.241	-0.109
Age	Number	Percent	Number	Percent	0.153	0.010
18-44 years	1,164	2.4%	8,502	2.5%	-0.153	-0.010
45-54 years	2,653	5.4%	18,293	5.4%	-0.028	-0.001
55-64 years	5,990	12.2%	40,547	12.0%	0.161	0.005
65+ years	39,333	80.0%	269,741	80.0%	0.021	0.001
Sex	40.000	20.40/	407.074	o/	46.600	
Female	19,226	39.1%	187,871	55.7%	-16.609	-0.337
Male	29,914	60.9%	149,212	44.3%	16.609	0.337
Race						
American Indian or Alaska Native	133	0.3%	1,948	0.6%	-0.307	-0.047
Asian	1,070	2.2%	7,811	2.3%	-0.140	-0.009
Black or African American	6,989	14.2%	55,801	16.6%	-2.331	-0.065
Native Hawaiian or Other Pacific Islander	61	0.1%	478	0.1%	-0.018	-0.005
Unknown	8,082	16.4%	47,793	14.2%	2.268	0.063
White	32,805	66.8%	223,252	66.2%	0.528	0.011
Hispanic Origin	1,135	2.3%	9,032	2.7%	-0.370	-0.024
Year						
2015	878	1.8%	32,231	9.6%	-7.775	-0.341
2016	6,685	13.6%	70,696	21.0%	-7.369	-0.196
2017	11,072	22.5%	73,800	21.9%	0.638	0.015
2018	13,611	27.7%	81,657	24.2%	3.474	0.079
2019	16,598	33.8%	77,594	23.0%	10.758	0.240
2020	296	4.9%	1,105	3.2%	1.652	0.084
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.4	2.7	5.8	3.0	-0.374	-0.133
Score ³						
	Number	Percent	Number	Percent		
Ambulatory allergies or allergy treatment	26,106	53.1%	169,522	50.3%	2.835	0.057
Angioedema (-183, -1)	58	0.1%	825	0.2%	-0.127	-0.030
Angioedema (ever, -1)	750	1.5%	7,357	2.2%	-0.656	-0.049
Diabetes	26,110	53.1%	173,497	51.5%	1.664	0.033
Ischemic heart disease	38,297	77.9%	203,944	60.5%	17.432	0.385
Renal disorders	21,237	43.2%	154,620	45.9%	-2.653	-0.053
Serious allergies	6,466	13.2%	54,435	16.1%	-2.991	-0.085

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Table 1m. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)

		Medical		Covariate Balance			
	S	SV.	A	CEI			
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference	
Ambulatory allergies or treatment and not serious allergies	21,703	44.2%	134,451	39.9%	4.279	0.087	
History of Use:							
Diuretics (thiazides, potassium sparing, loop diuretics)	42,889	87.3%	222,859	66.1%	21.165	0.517	
Everolimus	15	0.0%	98	0.0%	0.001	0.001	
Nonsteroidal anti-inflammatory drugs (NSAIDs)	5,633	11.5%	44,187	13.1%	-1.645	-0.050	
Sirolimus	****	****	142	0.0%	-0.030	-0.018	
		Standard		Standard			
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation			
Mean number of ambulatory encounters	19.2	14.8	20.4	22.5	-1.228	-0.064	
Mean number of emergency room encounters	0.6	1.3	0.8	1.7	-0.169	-0.112	
Mean number of inpatient hospital encounters	0.8	1.1	0.8	1.1	-0.079	-0.071	
Mean number of non-acute institutional encounters	0.2	0.7	0.4	1.0	-0.174	-0.192	
Mean number of other ambulatory encounters	8.1	11.6	11.7	17.4	-3.639	-0.246	
Mean number of filled prescriptions	32.5	20.9	27.8	22.3	4.697	0.217	
Mean number of generics	13.8	5.4	12.0	5.8	1.857	0.331	
Mean number of unique drug classes	12.0	4.7	11.2	5.1	0.812	0.164	

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requesterdefined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity sc ore predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Covariate Balance

Table 1n. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

Medical Product

		IVICUICAI			Covariate Balance		
	S	SV	A	CEI	Absolute	Standardized	
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference	
Patients (Number)	49,137	100.0%	49,137	14.6%	-	-	
		Standard		Standard			
Demographics	Mean	Deviation	Mean	Deviation			
Mean age (years)	72.6	10.7	72.6	11.5	-0.016	-0.001	
Age	Number	Percent	Number	Percent			
18-44 years	1,164	2.4%	1,231	2.5%	-0.136	-0.009	
45-54 years	2,652	5.4%	2,977	6.1%	-0.661	-0.029	
55-64 years	5,988	12.2%	6,682	13.6%	-1.412	-0.043	
65+ years	39,333	80.0%	38,247	77.8%	2.210	0.058	
Sex							
Female	19,226	39.1%	19,287	39.3%	-0.124	-0.003	
Male	29,911	60.9%	29,850	60.7%	0.124	0.003	
Race							
American Indian or Alaska Native	133	0.3%	144	0.3%	-0.022	-0.004	
Asian	1,070	2.2%	1,059	2.2%	0.022	0.002	
Black or African American	6,988	14.2%	7,004	14.3%	-0.033	-0.001	
Native Hawaiian or Other Pacific Islander	61	0.1%	53	0.1%	0.016	0.005	
Unknown	8,080	16.4%	8,091	16.5%	-0.022	-0.001	
White	32,805	66.8%	32,786	66.7%	0.039	0.001	
Hispanic Origin	1,135	2.3%	1,221	2.5%	-0.175	-0.011	
Year							
2015	878	1.8%	822	1.7%	0.114	0.009	
2016	6,685	13.6%	6,735	13.7%	-0.102	-0.003	
2017	11,072	22.5%	11,079	22.5%	-0.014	-0.000	
2018	13,611	27.7%	13,558	27.6%	0.108	0.002	
2019	16,595	33.8%	16,643	33.9%	-0.098	-0.002	
2020	296	4.9%	300	5.0%	-0.066	-0.003	
		Standard		Standard			
Recorded History of:	Mean	Deviation	Mean	Deviation			
Charlson/Elixhauser Combined Comorbidity	5.4	2.7	5.4	2.7	0.001	0.000	
Score ³							
	Number	Percent	Number	Percent			
Ambulatory allergies or allergy treatment	26,103	53.1%	26,126	53.2%	-0.047	-0.001	
Angioedema (-183, -1)	58	0.1%	56	0.1%	0.004	0.001	
Angioedema (ever, -1)	750	1.5%	1,084	2.2%	-0.680	-0.050	
Diabetes	26,109	53.1%	25,978	52.9%	0.267	0.005	
Ischemic heart disease	38,294	77.9%	38,161	77.7%	0.271	0.007	
Renal disorders	21,235	43.2%	21,281	43.3%	-0.094	-0.002	
Serious allergies	6,466	13.2%	6,500	13.2%	-0.069	-0.002	

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Table 1n. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical	Product		Covariate Balance			
	S	V	A	CEI				
Characteristic ^{1,2}	Number	Percent	Number	Percent	Absolute Difference	Standardized Difference		
Ambulatory allergies or treatment and not serious allergies	21,700	44.2%	21,734	44.2%	-0.069	-0.001		
History of Use:								
Diuretics (thiazides, potassium sparing, loop diuretics)	42,886	87.3%	42,937	87.4%	-0.104	-0.003		
Everolimus	15	0.0%	19	0.0%	-0.008	-0.004		
Nonsteroidal anti-inflammatory drugs (NSAIDs)	5,633	11.5%	5,752	11.7%	-0.242	-0.008		
Sirolimus	****	****	****	****	0.004	0.004		
		Standard		Standard				
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation				
Mean number of ambulatory encounters	19.2	14.8	19.2	19.8	-0.002	-0.000		
Mean number of emergency room encounters	0.6	1.3	0.6	1.2	-0.010	-0.008		
Mean number of inpatient hospital encounters	0.8	1.1	0.8	1.0	0.000	0.000		
Mean number of non-acute institutional encounters	0.2	0.7	0.2	0.7	-0.002	-0.002		
Mean number of other ambulatory encounters	8.1	11.6	8.1	11.0	0.006	0.001		
Mean number of filled prescriptions	32.5	20.9	29.7	22.4	2.717	0.125		
Mean number of generics	13.8	5.4	12.9	5.8	0.967	0.173		
Mean number of unique drug classes	12.0	4.7	12.0	5.1	-0.034	-0.007		

¹Covariates in italics were not included in the propensity score logistic regression model

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²Covariates in blue show a standardized difference greater than 0.1

³The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requesterdefined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity scor e predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 2. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

No. disal Dundasa	Number of	Person Years at	Average Person Days at			Incidence Rate per 1,000 Person		Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
Site-Adjusted Analysis SV (14-day gap, history of	69,639	****	****	****	****	2.14	****		****	0.00 / 0.00 .0 .00	2.221
ACEI (-183, -1)) ACEI (14-day gap)	694,882	****	****	****	****	6.74	****	-4.6	****	0.30 (0.23, 0.40)	<0.001
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	69,639	****	****	****	****	2.65	****	7.22	****	0.27 / 0.40 . 0.20	.0.004
ACEI (-183, -1)) ACEI (14-day gap)	69,639	****	****	****	****	9.87	****	-7.22	****	0.27 (0.19, 0.39)	<0.001
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	69,639	****	****	****	****	2.14	****				
ACEI (-183, -1))								-4.33	****	0.31 (0.23, 0.43)	<0.001
ACEI (14-day gap)	69,639	****	****	****	****	6.47	****				
Propensity Score Adjusted St	tratified Analy	ysis; Perce	ntiles= 10 ¹								
SV (14-day gap, history of	69,639	****	****	****	****	2.14	****				
ACEI (-183, -1))								-4.6	****	0.32 (0.24, 0.42)	<0.001
ACEI (14-day gap)	694,882	****	****	****	****	6.74	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 3. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
					Overall					•	
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	69,639	****	****	****	****	2.14	****	-4.6	****	0.30 (0.23, 0.40)	<0.001
ACEI (183-day prior, 14-day gap)	694,882	****	****	****	****	6.74	****	-4.0		0.30 (0.23, 0.40)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	69,639	****	****	****	****	2.65	****	7.22	****	0.27 / 0.40 . 0.20)	40 001
ACEI (183-day prior, 14-day gap)	69,639	****	****	****	****	9.87	****	-7.22		0.27 (0.19, 0.39)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	69,639	****	****	****	****	2.14	****	-4.33	****	0.31 (0.23, 0.43)	<0.001
ACEI (183-day prior, 14-day gap)	69,639	****	****	****	****	6.47	****	-4.55		0.31 (0.23, 0.43)	<0.001
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	69,639	****	****	****	****	3.49	****	-11.86	****	0.22 (0.14, 0.36)	<0.001
ACEI (183-day prior, 14-day gap)	694,882	****	****	****	****	15.35	****	11.00		0.22 (0.14, 0.30)	10.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	69,639	****	****	****	****	3.61	****	-15.66	****	0.19 (0.11, 0.31)	<0.001
ACEI (183-day prior, 14-day gap)	69,639	****	****	****	****	19.27	****	-13.00		0.19 (0.11, 0.31)	\0.001
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	69,639	****	****	****	****	3.49	****	-14.63	****	0.19 (0.12, 0.32)	<0.001
ACEI (183-day prior, 14-day gap)	69,639	****	****	****	****	18.12	****	-14.03		0.19 (0.12, 0.32)	\0.001
					31 - 60 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	55,796	****	****	****	****	3.17	****	-2.88	****	0.53 (0.29, 0.94)	0.029
ACEI (183-day prior, 14-day gap)	638,366	****	****	****	****	6.05	****	2.00		0.00 (0.20, 0.04)	0.025

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Table 3. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

		Person	Average Person	Average Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval)	P-Value
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹						·	
SV (183-day prior, 14-daygap)	51,126	****	****	****	****	3.59	****	1.2	****	0.72 / 0.24 1.60	0.425
ACEI (183-day prior, 14-daygap)	51,126	****	****	****	****	4.89	****	-1.3		0.73 (0.34, 1.60)	0.435
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-daygap)	55,796	****	****	****	****	3.17	****	-2.13	****	0.59 (0.30, 1.18)	0.137
ACEI (183-day prior, 14-daygap)	63,837	****	****	****	****	5.3	****	-2.15		0.39 (0.30, 1.16)	0.137
					61 - 90 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-daygap)	37,655	****	****	****	****	2.5	****	-3.29	****	0.43 (0.20, 0.92)	0.029
ACEI (183-day prior, 14-daygap)	462,969	****	****	****	****	5.78	****	-5.25		0.43 (0.20, 0.32)	0.023
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-daygap)	25,679	****	****	****	****	2.23	****	-3.35	****	0.40 (0.13, 1.28)	0.121
ACEI (183-day prior, 14-daygap)	25,679	****	****	****	****	5.58	****	-5.55		0.40 (0.13, 1.26)	0.121
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-daygap)	37,655	****	****	****	****	2.5	****	-3.02	****	0.45 (0.19, 1.07)	0.07
ACEI (183-day prior, 14-daygap)	47,340	****	****	****	****	5.52	****	-5.02		0.45 (0.13, 1.07)	0.07
				9	191 - 180 Day	rs .					
Site-Adjusted Analysis											
SV (183-day prior, 14-daygap)	30,271	****	****	****	****	0.52	****	-3.87	****	0.12 (0.04, 0.37)	<0.001
ACEI (183-day prior, 14-daygap)	397,712	****	****	****	****	4.39	****	<u> </u>		0.12 (0.04, 0.37)	·0.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-daygap)	17,788	****	****	****	****	0.4	****	-3.98	****	0.09 (0.01, 0.70)	0.022
ACEI (183-day prior, 14-daygap)	17,788	****	****	****	****	4.37	****	-3.30		0.03 (0.01, 0.70)	0.022

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Table 3. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

	Number of	Person Years	Average Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	• ,	Interval)	P-Value
Fixed Ratio 1:1 Propensity Score								10.00			1 10.00
SV (183-day prior, 14-daygap)	30,271	****	****	****	****	0.52	****	2.04	****	0.45 / 0.05 0.40\	0.003
ACEI (183-day prior, 14-daygap)	40,739	****	****	****	****	3.43	****	-2.91	4.4.4.4.4	0.15 (0.05, 0.49)	0.002
				18	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-daygap)	18,853	****	****	****	****	1.81	****	-2.31	****	0.44 (0.21, 0.93)	0.033
ACEI (183-day prior, 14-daygap)	235,524	****	****	****	****	4.12	****	-2.51		0.44 (0.21, 0.33)	0.055
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-daygap)	6,391	****	****	****	****	1.87	****	-1.87	****	0.50 (0.09, 2.73)	0.423
ACEI (183-day prior, 14-daygap)	6,391	****	****	****	****	3.73	****	-1.07		0.30 (0.03, 2.73)	0.423
Fixed Ratio 1:1 Propensity Score	Matched Unco										
SV (183-day prior, 14-daygap)	18,853	****	****	****	****	1.81	****	-1.18	****	0.60 (0.24, 1.49)	0.272
ACEI (183-day prior, 14-daygap)	23,569	****	****	****	****	2.99	****	-1.10		0.00 (0.24, 1.43)	0.272
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-daygap)	13,182	****	****	****	****	1.72	****	-1.83	****	0.48 (0.19, 1.16)	0.104
ACEI (183-day prior, 14-daygap)	164,756	****	****	****	****	3.54	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond		lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-daygap)	3,020	****	****	****	****	1.78	****	-1.78	****	0.50 (0.05, 5.51)	0.571
ACEI (183-day prior, 14-daygap)	3,020	****	****	****	****	3.55	****	1.70		0.55 (0.05, 5.51)	0.57 1
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-daygap)	13,182	****	****	****	****	1.72	****	0.25	****	1.16 (0.33, 3.99)	0.82
ACEI (183-day prior, 14-daygap)	15,799	****	****	****	****	1.47	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 4. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183,-1)

		Person	Average Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years at	Days at		Number	per 1,000 Person	•	1.000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	Interval)	P-Value
No Angioedema (-183, -1)		711011	11.011		0. 2. 00	1.00.10			11011 00010		
Site-Adjusted Analysis											
SV (14-day gap, history of	69,556	****	****	****	****	2.06	****				
ACEI (-183, -1))								-4.42	****	0.30 (0.23, 0.40)	<0.001
ACEI (14-day gap)	694,018	****	****	****	****	6.48	****				
Fixed Ratio 1:1 Propensity So	core Matched	Conditiona	l Analysis;	Caliper= 0	.05 ¹						
SV (14-day gap, history of	69,556	****	****	****	****	2.51	****				
ACEI (-183, -1))								-6.87	****	0.27 (0.18, 0.39)	<0.001
ACEI (14-day gap)	69,556	****	****	****	****	9.38	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditic	nal Analys	sis; Caliper	= 0.05						
SV (14-day gap, history of	69,556	****	****	****	****	2.06	****				
ACEI (-183, -1))								-4.14	****	0.32 (0.23, 0.43)	<0.001
ACEI (14-day gap)	69,556	****	****	****	****	6.2	****				
Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	83	****	****	****	****	72.23	****				
ACEI (-183, -1))								-195.97	****	0.28 (0.07, 1.13)	0.074
ACEI (14-day gap)	864	****	****	****	****	268.2	****				
Fixed Ratio 1:1 Propensity So	core Matched	Conditiona	l Analysis;	Caliper= 0	.05 ¹						
SV (14-day gap, history of	68	****	****	****	****	204.5	****				
ACEI (-183, -1))								-511.25	****	0.29 (0.06, 1.38)	0.118
ACEI (14-day gap)	68	****	****	****	****	715.75	****				
Fixed Ratio 1:1 Propensity So	core Matched			•							
SV (14-day gap, history of	68	****	****	****	****	90.13	****				
ACEI (-183, -1))								-293.22	****	0.30 (0.06, 1.44)	0.131
ACEI (14-day gap)	68	****	****	****	****	383.35	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time

		Person	Average Person	Average Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
No Angioedema (-183, -1)											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	69,556	****	****	****	****	2.06	****	-4.42	****	0.30 (0.23, 0.40)	<0.001
ACEI (183-day prior, 14-day gap)	694,018	****	****	****	****	6.48	****	7.72		0.50 (0.25, 0.40)	10.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	69,556	****	****	****	****	2.51	****	-6.87	****	0.27 (0.18, 0.39)	<0.001
ACEI (183-day prior, 14-day gap)	69,556	****	****	****	****	9.38	****	-0.87		0.27 (0.18, 0.39)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	69,556	****	****	****	****	2.06	****	-4.14	****	0.32 (0.23, 0.43)	<0.001
ACEI (183-day prior, 14-day gap)	69,556	****	****	****	****	6.2	****	-4.14		0.32 (0.23, 0.43)	<0.001
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	69,556	****	****	****	****	3.3	****	-11.18	****	0.22 (0.14, 0.36)	<0.001
ACEI (183-day prior, 14-day gap)	694,018	****	****	****	****	14.48	****	-11.10		0.22 (0.14, 0.36)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	69,556	****	****	****	****	3.42	****	44.47	****	0.40 (0.44 . 0.22)	.0.001
ACEI (183-day prior, 14-day gap)	69,556	****	****	****	****	17.89	****	-14.47	****	0.19 (0.11, 0.32)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	69,556	****	****	****	****	3.3	****	12.57	****	0.10 / 0.12 . 0.22)	10.001
ACEI (183-day prior, 14-day gap)	69,556	****	****	****	****	16.87	****	-13.57		0.19 (0.12, 0.33)	<0.001
					31 - 60 Days	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	55,726	****	****	****	****	2.91	****	-2.83	****	0.51 (0.28, 0.93)	0.028
ACEI (183-day prior, 14-day gap)	637,620	****	****	****	****	5.74	****	-2.05		0.31 (0.26, 0.93)	0.026
Fixed Ratio 1:1 Propensity Score	Matabad Cana	litional Ana	lycic. Calin	er= 0.05 ¹							
Tixed Matio 1:11 Topensity Score	watched Cond	iitiOnai Ana	iysis, calipi	cı – 0.03							
SV (183-day prior, 14-day gap)	51,069	*****	****	****	****	3.26	****	-1.63	****	0.67 (0.30, 1.48)	0.321

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Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time

		Person	Person	Average Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio	W-14
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	55,726	****	****	****	****	2.91	****	-2.18	****	0.57 (0.28, 1.16)	0.12
ACEI (183-day prior, 14-day gap)	63,770	****	****	****	****	5.08	****	-2.10		0.57 (0.26, 1.10)	0.12
					61 - 90 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	37,612	****	****	****	****	2.5	****	2.45	****	0.44/0.31 0.04)	0.034
ACEI (183-day prior, 14-day gap)	462,481	****	****	****	****	5.65	****	-3.15		0.44 (0.21, 0.94)	0.034
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip								
SV (183-day prior, 14-day gap)	25,660	****	****	****	****	2.23	****	-3.35	****	0.40 (0.13, 1.28)	0.121
ACEI (183-day prior, 14-day gap)	25,660	****	****	****	****	5.59	****	-5.55		0.40 (0.13, 1.28)	0.121
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	37,612	****	****	****	****	2.5	****	2.02	****	0.45 / 0.10 1.07)	0.07
ACEI (183-day prior, 14-day gap)	47,301	****	****	****	****	5.52	****	-3.02		0.45 (0.19, 1.07)	0.07
				9	91 - 180 Day	/s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	30,241	****	****	****	****	0.52	****	2.0	****	0.13 / 0.04 0.39)	<0.001
ACEI (183-day prior, 14-day gap)	397,313	****	****	****	****	4.33	****	-3.8		0.12 (0.04, 0.38)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	17,775	****	****	****	****	0.4	****	3.00	****	0.00 / 0.01 0.70	0.022
ACEI (183-day prior, 14-day gap)	17,775	****	****	****	****	4.38	****	-3.98	and the same and	0.09 (0.01, 0.70)	0.022

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Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	Number of New Users Matched Unco 30,241	Person Years at Risk nditional A	Average Person Days at Risk nalysis; Ca	Average Person Years at Risk liper= 0.05	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years		Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
ACEI (183-day prior, 14-day gap)	40,704	****	****	****	****	3.43	****	-2.91	****	0.15 (0.05, 0.49)	0.002
recti (100 day prior, 14 day gap)	40,704			18	81 - 270 Da						
Site-Adjusted Analysis						•					
SV (183-day prior, 14-day gap)	18,831	****	****	****	****	1.81	****	-2.27	****	0.44 / 0.21 . 0.04)	0.035
ACEI (183-day prior, 14-day gap)	235,324	****	****	****	****	4.08	****	-2.27		0.44 (0.21, 0.94)	0.035
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	6,379	****	****	****	****	1.87	****	-1.87	****	0.50 (0.09, 2.73)	0.423
ACEI (183-day prior, 14-day gap)	6,379	****	****	****	****	3.74	****	-1.87		0.50 (0.09, 2.73)	0.423
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05							
SV (183-day prior, 14-day gap)	18,831	****	****	****	****	1.81	****	-1.18	****	0.60 (0.24, 1.49)	0.272
ACEI (183-day prior, 14-day gap)	23,552	****	****	****	****	2.99	****	-1.10		0.00 (0.24, 1.49)	0.272
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	13,165	****	****	****	****	1.72	****	-1.75	****	0.49 (0.20, 1.19)	0.115
ACEI (183-day prior, 14-day gap)	164,613	****	****	****	****	3.47	****	2.,5		0.15 (0.20, 1.15)	
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	3,013	****	****	****	****	1.78	****	-1.78	****	0.50 (0.05, 5.51)	0.571
ACEI (183-day prior, 14-day gap)	3,013	****	****	****	****	3.55	****	-1.70		0.50 (0.05, 5.51)	0.5/1
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.05		•					
SV (183-day prior, 14-day gap)	13,165	****	****	****	****	1.72	****	0.25	****	1.15 (0.33, 3.99)	0.82
ACEI (183-day prior, 14-day gap)	15,786	****	****	****	****	1.47	****	0.23		1.13 (0.33, 3.33)	0.02

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Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Angioedema (-183, -1)					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	83	****	****	****	****	72.23	****		****		
ACEI (183-day prior, 14-day gap)	864	****	****	****	****	268.2	****	-195.97	****	0.28 (0.07, 1.13)	0.074
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	68	****	****	****	****	204.5	****	F44.2F	****	0.30 / 0.05 (1.30)	0.110
ACEI (183-day prior, 14-day gap)	68	****	****	****	****	715.75	****	-511.25	4.4.4.4.4	0.29 (0.06, 1.38)	0.118
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	68	****	****	****	****	90.13	****	-293.22	****	0.30 (0.06, 1.44)	0.131
ACEI (183-day prior, 14-day gap)	68	****	****	****	****	383.35	****	-293.22		0.30 (0.06, 1.44)	0.131
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	83	****	****	****	****	158.98	****	-582.21	****	0.21 (0.03, 1.49)	0.118
ACEI (183-day prior, 14-day gap)	864	****	****	****	****	741.19	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond										
SV (183-day prior, 14-day gap)	68	****	****	****	****	203.25	****	-1016.26	****	0.17 (0.02, 1.38)	0.097
ACEI (183-day prior, 14-day gap)	68	****	****	****	****	1,219.51	****	1010.20		0.17 (0.02, 1.30)	0.037
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	68	****	****	****	****	191.94	****	-940.14	****	0.17 (0.02, 1.42)	0.102
ACEI (183-day prior, 14-day gap)	68	****	****	****	****	1,132.08	****				
					31 - 60 Day	S					
Site-Adjusted Analysis	70	****	****	****	****	245.00	****				
SV (183-day prior, 14-day gap)	70	****	****	****	****	215.98	****	-60.81	****	0.85 (0.11, 6.49)	0.876
ACEI (183-day prior, 14-day gap)	749				**************************************	276.79	ar ar ar ar W				
Fixed Ratio 1:1 Propensity Score		litional Ana	llysis; Calip	er= 0.05 ⁻	****	247.22	****				
SV (183-day prior, 14-day gap)	50	****	****	****	****	347.22	****	0	****	1.00 (0.06, 15.99)	1
ACEI (183-day prior, 14-day gap)	50	****	ተተ ችችች	ጥጥ ጥጥ ጥ	****	347.22	ጥጥ ጥጥ			,	

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Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time

			Average	Average		Incidence Rate per	Risk per	Incidence Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!							
SV (183-day prior, 14-day gap)	57	****	****	****	****	261.78	****	16.08	****	1.11 (0.07, 17.85)	0.939
ACEI (183-day prior, 14-day gap)	61	****	****	****	****	245.7	****	10.08		1.11 (0.07, 17.83)	0.333
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	45	****	****	****	****	0	****	-136.2	****		
ACEI (183-day prior, 14-day gap)	490	****	****	****	****	136.2	****	-130.2		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Cond		lysis; Calip								
SV (183-day prior, 14-day gap)	22	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	22	****	****	****	****	0	****	0		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	35	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	38	****	****	****	****	0	****	0		<u>-</u>	
				9	91 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	32	****	****	****	****	0	****	-73.62	****	_	_
ACEI (183-day prior, 14-day gap)	402	****	****	****	****	73.62	****	-73.02			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	14	****	****	****	****	0	****		****		
ACEI (183-day prior, 14-day gap)	14	****	****	****	****	0	****	0		-	-

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Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time

ACEI (183-day prior, 14-day gap) 33 ***** **** ***** 0 ***** 181 - 270 Days	
,	
Cita Adiustad Analysia	
Site-Adjusted Analysis SV (183-day prior, 14-day gap) 22 ***** ***** 0 *****	
3v (165-uay prior, 14-uay gap) 22 -47 33 ***** -	-
ACE (105-uay prior, 14-uay gap) 203 47.55	
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ¹	
SV (183-day prior, 14-day gap) ***** **** **** ***** 0 ***** 0 *****	_
ACEI (183-day prior, 14-day gap)	
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05	
SV (183-day prior, 14-day gap) 20 ***** **** ***** 0 ***** 0 *****	
ACEI (183-day prior, 14-day gap) 11 ***** ***** ***** 0 *****	
271 - 365 Days	
Site-Adjusted Analysis	
SV (183-day prior, 14-day gap) 18 ***** **** ***** 0 ***** -92.65 ****	
ACEI (183-day prior, 14-day gap) 148 ***** ***** ***** 92.65 *****	
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ¹	
SV (183-day prior 14-day gan) ***** **** **** ***** 0 *****	
ACEI (183-day prior, 14-day gap) ***** ***** ***** 0 *****	-
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05	
SV (183-day prior, 14-day gap) 16 ***** **** ***** 0 *****	
ACEI (183-day prior, 14-day gap) ***** ***** ***** 0 ***** -	-

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 6. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)

-1		Person	Average Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
Madical Duaduct	Number of	Years at	Days at			per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product No Angioedema (ever, -1)	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
Site-Adjusted Analysis		_	_	_	_		_				_
SV (14-day gap, history of	69,145	****	****	****	****	1.99	****				
ACEI (-183, -1))	03,143					1.55		-3.89	****	0.32 (0.24, 0.43)	< 0.001
ACEI (165, 1), ACEI (14-day gap)	687,565	****	****	****	****	5.88	****	0.00		0.02 (0.2 ., 00,	10.002
Fixed Ratio 1:1 Propensity So		Conditiona	l Analysis	Caliner= C	0.051	3.00					
SV (14-day gap, history of	69,144	****	****	****	****	2.38	****				
ACEI (-183, -1))	33,2							-6.12	****	0.28 (0.19, 0.41)	< 0.001
ACEI (14-day gap)	69,144	****	****	****	****	8.5	****			, , ,	
Fixed Ratio 1:1 Propensity So		Unconditic	nal Analys	is; Caliper	= 0.05						
SV (14-day gap, history of	69,144	****	****	****	****	1.99	****				
ACEI (-183, -1))								-3.59	****	0.34 (0.25, 0.47)	< 0.001
ACEI (14-day gap)	69,144	****	****	****	****	5.58	****				
Angioedema (ever, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	494	****	****	****	****	25.6	****				
ACEI (-183, -1))								-71.51	****	0.25 (0.09, 0.67)	0.006
ACEI (14-day gap)	7,317	****	****	****	****	97.12	****				
Fixed Ratio 1:1 Propensity So	core Matched	Conditiona	l Analysis;	Caliper= C).05 ¹						
SV (14-day gap, history of	487	****	****	****	****	24.08	****				
ACEI (-183, -1))								-120.42	****	0.17 (0.04, 0.74)	0.019
ACEI (14-day gap)	487	****	****	****	****	144.51	****				
Fixed Ratio 1:1 Propensity So											
SV (14-day gap, history of	487	****	****	****	****	25.94	****				
ACEI (-183, -1))								-86.94	****	0.23 (0.08, 0.68)	0.008
ACEI (14-day gap)	487	****	****	****	****	112.88	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 7. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies

			Average	Average	•	•	Risk per	Incidence Rate	Difference		
		Person	Person	Person		Incidence Rate	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at	Number	per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
No Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	61,592	****	****	****	****	2.08	****				
ACEI (-183, -1))								-4.4	****	0.31 (0.23, 0.41)	< 0.001
ACEI (14-day gap)	583,922	****	****	****	****	6.47	****				
Fixed Ratio 1:1 Propensity So	core Matched	Conditiona	ıl Analysis;	Caliper= 0	.05 ¹						
SV (14-day gap, history of	61,582	****	****	****	****	2.4	****				
ACEI (-183, -1))								-6.08	****	0.28 (0.19, 0.42)	< 0.001
ACEI (14-day gap)	61,582	****	****	****	****	8.47	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditio	nal Analys	sis; Caliper	= 0.05						
SV (14-day gap, history of	61,582	****	****	****	****	2.08	****				
ACEI (-183, -1))								-3.7	****	0.34 (0.25, 0.48)	< 0.001
ACEI (14-day gap)	61,582	****	****	****	****	5.77	****				
Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	8,047	****	****	****	****	2.69	****				
ACEI (-183, -1))								-5.63	****	0.31 (0.15, 0.66)	0.002
ACEI (14-day gap)	110,960	****	****	****	****	8.32	****				
Fixed Ratio 1:1 Propensity So	core Matched	Conditiona	l Analysis;	Caliper= C	.05 ¹						
SV (14-day gap, history of	8,038	****	****	****	****	3.46	****				
ACEI (-183, -1))								-7.61	****	0.31 (0.11, 0.85)	0.023
ACEI (14-day gap)	8,038	****	****	****	****	11.07	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditio	nal Analys	sis; Caliper	= 0.05						
SV (14-day gap, history of	8,038	****	****	****	****	2.69	****				
ACEI (-183, -1))								-4.38	****	0.36 (0.15, 0.85)	0.02
ACEI (14-day gap)	8,038	****	****	****	****	7.07	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



<u> </u>	•		Average		<u>,, ,</u>		Risk per	Incidence Rate	Difference		
		Person	Person	Person	Number	Incidence	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Sex: Male											
					Overal	l					
Site-Adjusted Analysis											
SV (14-day gap, history of	48,440	****	****	****	****	2.4	****				
ACEI (-183, -1))								-3.58	****	0.38 (0.28, 0.52)	<0.001
ACEI (14-day gap)	353,015	****	****	****	****	5.98	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	48,398	****	****	****	****	2.67	****				
ACEI (-183, -1))								-5.84	****	0.31 (0.20, 0.49)	< 0.001
ACEI (14-day gap)	48,398	****	****	****	****	8.51	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor										
SV (14-day gap, history of	48,398	****	****	****	****	2.4	****				
ACEI (-183, -1))								-2.99	****	0.43 (0.30, 0.61)	<0.001
ACEI (14-day gap)	48,398	****	****	****	****	5.39	****				
					0 - 30 Da	ıys					
Site-Adjusted Analysis											
SV (14-day gap, history of	48,440	****	****	****	****	3.06	****			,	
ACEI (-183, -1))								-11.55	****	0.21 (0.11, 0.38)	<0.001
ACEI (14-day gap)	353,015	****	****	****	****	14.61	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.051							
SV (14-day gap, history of	48,398	****	****	****	****	2.88	****				
ACEI (-183, -1))								-12.96	****	0.18 (0.09, 0.36)	<0.001
ACEI (14-day gap)	48,398	****	****	****	****	15.85	****				
Fixed Ratio 1:1 Propensity Score											
SV (14-day gap, history of	48,398	****	****	****	****	3.06	****				
ACEI (-183, -1))								-12.32	****	0.20 (0.10, 0.38)	<0.001
ACEI (14-day gap)	48,398	****	****	****	****	15.38	****				

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, ,	, , ,		Average				Risk per	Incidence Rate	Difference		
		Person	Person	Person	Number	Incidence	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					31 - 60 D	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	39,001	****	****	****	****	3.76	****				
ACEI (-183, -1))								-1.83	****	0.67 (0.35, 1.27)	0.22
ACEI (14-day gap)	325,549	****	****	****	****	5.59	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	35,714	****	****	****	****	4.19	****				
ACEI (-183, -1))								-0.93	****	0.82 (0.34, 1.97)	0.655
ACEI (14-day gap)	35,714	****	****	****	****	5.12	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	38,972	****	****	****	****	3.77	****				
ACEI (-183, -1))								-0.03	****	0.97 (0.42, 2.25)	0.948
ACEI (14-day gap)	44,405	****	****	****	****	3.8	****				
					61 - 90 D	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	26,480	****	****	****	****	3.54	****				
ACEI (-183, -1))								-1.19	****	0.75 (0.35, 1.63)	0.47
ACEI (14-day gap)	236,720	****	****	****	****	4.74	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	18,101	****	****	****	****	3.95	****				
ACEI (-183, -1))								-3.95	****	0.50 (0.17, 1.46)	0.206
ACEI (14-day gap)	18,101	****	****	****	****	7.91	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	26,460	****	****	****	****	3.55	****				
ACEI (-183, -1))								-2.76	****	0.56 (0.23, 1.37)	0.205
ACEI (14-day gap)	33,143	****	****	****	****	6.31	****				

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			Average	Average			Risk per	Incidence Rate	Difference		
		Person	Person	Person	Number	Incidence	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					91 - 180 [Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	21,352	****	****	****	****	0.25	****				_
ACEI (-183, -1))								-3.26	****	0.07 (0.01, 0.50)	0.008
ACEI (14-day gap)	203,872	****	****	****	****	3.5	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi	tional Analy	ysis; Calipe	r= 0.05 ¹							
SV (14-day gap, history of	12,542	****	****	****	****	0	****				
ACEI (-183, -1))								-2.84	****	-	-
ACEI (14-day gap)	12,542	****	****	****	****	2.84	****				
Fixed Ratio 1:1 Propensity Score	e Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	21,337	****	****	****	****	0.25	****				
ACEI (-183, -1))								-2.51	****	0.09 (0.01, 0.66)	0.018
ACEI (14-day gap)	28,497	****	****	****	****	2.75	****				
					181 - 270	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	13,288	****	****	****	****	2.57	****				
ACEI (-183, -1))								-0.83	****	0.75 (0.35, 1.63)	0.469
ACEI (14-day gap)	120,238	****	****	****	****	3.41	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi										
SV (14-day gap, history of	4,429	****	****	****	****	1.37	****				
ACEI (-183, -1))								-1.37	****	0.50 (0.05, 5.51)	0.571
ACEI (14-day gap)	4,429	****	****	****	****	2.74	****				
Fixed Ratio 1:1 Propensity Score	e Matched Uncor										
SV (14-day gap, history of	13,277	****	****	****	****	2.58	****				
ACEI (-183, -1))								1.04	****	1.64 (0.52, 5.16)	0.399
ACEI (14-day gap)	16,416	****	****	****	****	1.54	****				

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Distributed Database (SDD) be	tweeli July 7, 201.	J allu rebiu	Average		is Type, s	ex and Follow-u	Risk per	Incidence Rate	Difference		
		Person	Person	Person	Number	Incidence	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years		Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	Days at Risk	at Risk	Events	Person Years		Person Years	New Users	Interval) ²	P-Value ²
Wedical Product	New Osers	at RISK	at RISK		271 - 365 I		Users	Person rears	New Osers	intervaij	P-value
Site-Adjusted Analysis					2/1 - 303	Days					
SV (14-day gap, history of	9,303	****	****	****	****	2.43	****				
ACEI (-183, -1))	3,303					2.43		-0.48	****	0.81 (0.33, 2.03)	0.658
ACEI (14-day gap)	84,117	****	****	****	****	2.91	****	51.15		0.01 (0.00) 1.00)	0.000
Fixed Ratio 1:1 Propensity Sco		tional Analy	rsis: Calina	- 0.05 ¹		2.31					
SV (14-day gap, history of	2,042	****	*****	****	****	2.65	****				
ACEI (-183, -1))	2,042					2.03		2.65	****	_	_
ACEI (14-day gap)	2,042	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sco		nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	9,299	****	****	****	****	2.43	****				
ACEI (-183, -1))	,							1.16	****	1.87 (0.45, 7.84)	0.39
ACEI (14-day gap)	10,933	****	****	****	****	1.27	****				
Sex: Female											
					Overal	I					
Site-Adjusted Analysis											
SV (14-day gap, history of	21,199	****	****	****	****	1.52	****				
ACEI (-183, -1))								-6	****	0.19 (0.11, 0.35)	<0.001
ACEI (14-day gap)	341,867	****	****	****	****	7.53	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi		sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	21,198	****	****	****	****	2.47	****				
ACEI (-183, -1))								-9.38	****	0.21 (0.11, 0.41)	<0.001
ACEI (14-day gap)	21,198	****	****	****	****	11.84	****				
Fixed Ratio 1:1 Propensity Sco											
SV (14-day gap, history of	21,198	****	****	****	****	1.52	****		****	0.40 / 0.40 . 0.05	0.004
ACEI (-183, -1))		ala ala ala ala	ala ala ala ala ala	ale ale ale ale ale	ale ale ale ale		ala ala ala ala ala	-6.1	****	0.19 (0.10, 0.36)	<0.001
ACEI (14-day gap)	21,198	****	****	****	****	7.62	****				
Site Adjusted Analysis					0 - 30 Da	iys					
Site-Adjusted Analysis	21 100	****	****	****	****	4.40	****				
SV (14-day gap, history of	21,199	-aaaaa	40.00.00.00.00	40.40.40.40.40	and the same of	4.49	40.00.00.00.00	-11.64	****	0.27 (0.13, 0.58)	<0.001
ACEI (-183, -1))	2/1 067	****	****	****	****	16.13	****	-11.04		0.27 (0.13, 0.36)	\U.UU1
ACEI (14-day gap)	341,867		• • :::::::::::::::::::::::::::::::::::			10.13					

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Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel

Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time

			Average	Average	_		Risk per	Incidence Rate	Difference	Hannal Bakin	
		Person	Person	Person	Number	Incidence	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Condi	itional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	21,198	****	****	****	****	4.65	****				
ACEI (-183, -1))								-17.95	****	0.21 (0.09, 0.46)	<0.001
ACEI (14-day gap)	21,198	****	****	****	****	22.6	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	21,198	****	****	****	****	4.49	****				
ACEI (-183, -1))								-16.99	****	0.21 (0.09, 0.46)	< 0.001
ACEI (14-day gap)	21,198	****	****	****	****	21.48	****				
					31 - 60 D	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	16,795	****	****	****	****	1.77	****				
ACEI (-183, -1))								-4.76	****	0.27 (0.07, 1.11)	0.069
ACEI (14-day gap)	312,817	****	****	****	****	6.52	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	itional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	15,272	****	****	****	****	2.23	****				
ACEI (-183, -1))								-3.34	****	0.40 (0.08, 2.06)	0.273
ACEI (14-day gap)	15,272	****	****	****	****	5.57	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	16,794	****	****	****	****	1.77	****				
ACEI (-183, -1))								-4.9	****	0.27 (0.06, 1.23)	0.09
ACEI (14-day gap)	19,286	****	****	****	****	6.66	****				

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			Average	Average			Risk per	Incidence Rate	Difference		
		Person	Person	Person	Number	Incidence	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					61 - 90 D	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	11,175	****	****	****	****	0	****				
ACEI (-183, -1))								-6.88	****	-	-
ACEI (14-day gap)	226,249	****	****	****	****	6.88	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi	tional Analy	/sis; Calipe	r= 0.05 ¹							
SV (14-day gap, history of	7,313	****	****	****	****	0	****				
ACEI (-183, -1))								-3.97	****	-	-
ACEI (14-day gap)	7,313	****	****	****	****	3.97	****				
Fixed Ratio 1:1 Propensity Score	e Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	11,174	****	****	****	****	0	****				
ACEI (-183, -1))								-2.83	****	-	-
ACEI (14-day gap)	13,934	****	****	****	****	2.83	****				
					91 - 180 [Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	8,919	****	****	****	****	1.18	****				
ACEI (-183, -1))								-4.13	****	0.22 (0.05, 0.89)	0.034
ACEI (14-day gap)	193,840	****	****	****	****	5.31	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi	tional Analy		r= 0.05 ¹							
SV (14-day gap, history of	4,920	****	****	****	****	1.43	****				
ACEI (-183, -1))								-5.74	****	0.20 (0.02, 1.71)	0.142
ACEI (14-day gap)	4,920	****	****	****	****	7.17	****				
Fixed Ratio 1:1 Propensity Score	e Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	8,918	****	****	****	****	1.18	****				
ACEI (-183, -1))								-3.07	****	0.28 (0.06, 1.28)	0.101
ACEI (14-day gap)	11,847	****	****	****	****	4.25	****				

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` '			Average	Average			Risk per	Incidence Rate	Difference		
		Davage	_	_	Number	Incidence	1,000			Hazard Ratio	
		Person	Person	Person	Number		•	Difference per	in Risk per	(95% Confidence	Wald
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	•	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					181 - 270	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	5,565	****	****	****	****	0	****				
ACEI (-183, -1))								-4.87	****	-	-
ACEI (14-day gap)	115,286	****	****	****	****	4.87	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi	itional Analy	ysis; Calipeı	r= 0.05 ¹							
SV (14-day gap, history of	1,759	****	****	****	****	0	****				
ACEI (-183, -1))								-6.82	****	-	-
ACEI (14-day gap)	1,759	****	****	****	****	6.82	****				
Fixed Ratio 1:1 Propensity Score	e Matched Unco	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	5,565	****	****	****	****	0	****				
ACEI (-183, -1))								-5.21	****	-	-
ACEI (14-day gap)	6,776	****	****	****	****	5.21	****				
					271 - 365	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	3,879	****	****	****	****	0	****				
ACEI (-183, -1))								-4.21	****	-	-
ACEI (14-day gap)	80,639	****	****	****	****	4.21	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi	itional Analy	ysis; Calipe	r= 0.05 ¹							
SV (14-day gap, history of	834	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	834	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score		nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	3,882	****	****	****	****	0	****				
ACEI (-183, -1))	•							-1.02	****	-	-
ACEI (14-day gap)	4,528	****	****	****	****	1.02	****				
¹Conditional analysis assounts for i		l +:				-					

¹Conditional analysis accounts for informative events and person-time.

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² Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 9. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

		Person	Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at		per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
Age Group: 18-44 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	2,412	****	****	****	****	1.3	****				
ACEI (-183, -1))								-7.86	****	0.14 (0.02, 1.03)	0.053
ACEI (14-day gap)	21,587	****	****	****	****	9.15	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	2,385	****	****	****	****	2.49	****				
ACEI (-183, -1))								-4.99	****	0.33 (0.03, 3.20)	0.341
ACEI (14-day gap)	2,385	****	****	****	****	7.48	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	2,385	****	****	****	****	1.31	****				
ACEI (-183, -1))								-3.65	****	0.25 (0.03, 2.28)	0.221
ACEI (14-day gap)	2,385	****	****	****	****	4.96	****				
Age Group: 45-54 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	5,115	****	****	****	****	2.92	****				
ACEI (-183, -1))								-7.36	****	0.28 (0.12, 0.69)	0.006
ACEI (14-day gap)	45,057	****	****	****	****	10.28	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	0.051						
SV (14-day gap, history of	5,075	****	****	****	****	3.26	****				
ACEI (-183, -1))	,							-9.79	****	0.25 (0.07, 0.89)	0.032
ACEI (14-day gap)	5,075	****	****	****	****	13.05	****			,	
Fixed Ratio 1:1 Propensity Sc		Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	5,075	****	****	****	****	2.94	****				
ACEI (-183, -1))	,							-6.18	****	0.31 (0.11, 0.84)	0.022
ACEI (14-day gap)	5,075	****	****	****	****	9.12	****			,	

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Table 9. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	Interval)	P-Value
Age Group: 55-64 Years	THE WOODERS	11.51	11.51	11.01.	UI EVEITE	1.0013	G 00.10	10015	new esers	ter tury	· value
Site-Adjusted Analysis											
SV (14-day gap, history of	11,494	****	****	****	****	2.62	****				
ACEI (-183, -1))	,							-6.32	****	0.29 (0.15, 0.54)	< 0.001
ACEI (14-day gap)	97,244	****	****	****	****	8.94	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	11,435	****	****	****	****	3.76	****				
ACEI (-183, -1))	,							-7.98	****	0.32 (0.14, 0.71)	0.005
ACEI (14-day gap)	11,435	****	****	****	****	11.74	****				
Fixed Ratio 1:1 Propensity So	core Matched	Uncondit	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	11,435	****	****	****	****	2.63	****				
ACEI (-183, -1))								-5.81	****	0.30 (0.15, 0.61)	<0.001
ACEI (14-day gap)	11,435	****	****	****	****	8.44	****				
Age Group: 65+ Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	50,618	****	****	****	****	2	****				
ACEI (-183, -1))								-4.03	****	0.32 (0.23, 0.44)	<0.001
ACEI (14-day gap)	530,994	****	****	****	****	6.03	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.051						
SV (14-day gap, history of	50,470	****	****	****	****	2.2	****				
ACEI (-183, -1))								-5.56	****	0.28 (0.18, 0.45)	< 0.001
ACEI (14-day gap)	50,470	****	****	****	****	7.76	****				
Fixed Ratio 1:1 Propensity So	core Matched	Uncondit		ysis; Calipe	er= 0.05						
SV (14-day gap, history of	50,470	****	****	****	****	2.01	****				
ACEI (-183, -1))								-3.06	****	0.38 (0.26, 0.55)	< 0.001
ACEI (14-day gap)	50,470	****	****	****	****	5.07	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Age Group: 18-44	_	_	_		Overall		_	_			
Site-Adjusted Analysis					O TOTAL						
SV (183-day prior, 14-day gap)	2,412	****	****	****	****	1.3	****	7.00	****	0.11/0.00 1.00	0.050
ACEI (183-day prior, 14-day gap)	21,587	****	****	****	****	9.15	****	-7.86	****	0.14 (0.02, 1.03)	0.053
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,385	****	****	****	****	2.49	****	4.00	****	0.22 / 0.02 2.20	0.244
ACEI (183-day prior, 14-day gap)	2,385	****	****	****	****	7.48	****	-4.99	****	0.33 (0.03, 3.20)	0.341
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	2,385	****	****	****	****	1.31	****	-3.65	****	0.25 (0.03, 2.28)	0.221
ACEI (183-day prior, 14-day gap)	2,385	****	****	****	****	4.96	****	-3.03		0.23 (0.03, 2.28)	0.221
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,412	****	****	****	****	0	****	-18.03	****	_	-
ACEI (183-day prior, 14-day gap)	21,587	****	****	****	****	18.03	****				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	2,385	****	****	****	****	0	****	-17.89	****	_	_
ACEI (183-day prior, 14-day gap)	2,385	****	****	****	****	17.89	****				
Fixed Ratio 1:1 Propensity Score			•	•							
SV (183-day prior, 14-day gap)	2,385	****	****	****	****	0	****	-15.97	****	-	_
ACEI (183-day prior, 14-day gap)	2,385	****	****	****	****	15.97	****				
City Adiabat Analysis					31 - 60 Day	S					
Site-Adjusted Analysis	1.000	****	****	****	****	7.02	****				
SV (183-day prior, 14-day gap)	1,896	****	****	****	****	7.93 8.33	****	-0.4	****	1.00 (0.13, 7.77)	0.998
ACEI (183-day prior, 14-day gap)	19,995					8.33					
Fixed Ratio 1:1 Propensity Score		itional Ana	lysis; Calip	er= 0.05 ⁻	****	10.46	****				
SV (183-day prior, 14-day gap)	1,698	****	****	****	****	10.46	****	10.46	****	-	-
ACEI (183-day prior, 14-day gap)	1,698	****	~~~ ^	~~~~	****	0	ጥጥጥ ጥ				

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

		Damasa	U	Average Person		Incidence Rate per	Risk per	Incidence Rate Difference	Difference in Risk	Hazard Ratio	
	Number of	Person	Person		Neumahau	1,000	1,000		_	(95% Confidence	Wald
Madical Duadocat		Years	Days	Years	Number	Person	New	per 1,000	per 1,000		
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score				-							
SV (183-day prior, 14-day gap)	1,880	****	****	****	****	8	****	8	****	_	_
ACEI (183-day prior, 14-day gap)	2,154	****	****	****	****	0	****	0			
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,216	****	****	****	****	0	****	-7.42	****		
ACEI (183-day prior, 14-day gap)	12,614	****	****	****	****	7.42	****	-7.42		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	719	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	719	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	1,204	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	1,414	****	****	****	****	0	****	0		-	
				9	1 - 180 Day	rs .					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	966	****	****	****	****	0	****	-5.85	****		_
ACEI (183-day prior, 14-day gap)	10,169	****	****	****	****	5.85	****	-5.65		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	441	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	441	****	****	****	****	0	****	0	and the same and	-	-

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

Medical Product Fixed Ratio 1:1 Propensity Score		Person Years at Risk onditional A	Average Person Days at Risk analysis; Ca	Average Person Years at Risk liper= 0.0	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap) ACEI (183-day prior, 14-day gap)	956 1,139	****	****	****	****	0	****	0	****	-	-
ACEI (165-day prior, 14-day gap)	1,139				81 - 270 Da						
Site-Adjusted Analysis					01 270 Da	y 3					
SV (183-day prior, 14-day gap)	562	****	****	****	****	0	****				
ACEI (183-day prior, 14-day gap)	5,183	****	****	****	****	7.89	****	-7.89	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	141	****	****	****	****	0	****		****		
ACEI (183-day prior, 14-day gap)	141	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	555	****	****	****	****	0	****	0.27	****		
ACEI (183-day prior, 14-day gap)	573	****	****	****	****	9.27	****	-9.27		-	<u>-</u>
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	383	****	****	****	****	0	****	-1.38	****	_	_
ACEI (183-day prior, 14-day gap)	3,344	****	****	****	****	1.38	****	1.50			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	59	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	59	****	****	****	****	0	****				_
Fixed Ratio 1:1 Propensity Score	Matched Unco		<u> </u>	•							
SV (183-day prior, 14-day gap)	378	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	353	****	****	****	****	0	****	0			

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

	Number of	Person Years	Average Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	• •	Interval) ²	P-Value ²
Age Group: 45-54											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	5,115	****	****	****	****	2.92	****	-7.36	****	0.28 (0.12, 0.69)	0.006
ACEI (183-day prior, 14-day gap)	45,057	****	****	****	****	10.28	****	-7.50		0.28 (0.12, 0.69)	0.006
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	5,075	****	****	****	****	3.26	****	0.70	****	0.35 / 0.07 0.00	0.033
ACEI (183-day prior, 14-day gap)	5,075	****	****	****	****	13.05	****	-9.79		0.25 (0.07, 0.89)	0.032
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	5,075	****	****	****	****	2.94	****	-6.18	****	0.31 (0.11, 0.84)	0.022
ACEI (183-day prior, 14-day gap)	5,075	****	****	****	****	9.12	****	-0.16		0.51 (0.11, 0.64)	0.022
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	5,115	****	****	****	****	5.27	****	-18.42	****	0.22 (0.05, 0.89)	0.033
ACEI (183-day prior, 14-day gap)	45,057	****	****	****	****	23.69	****	10.72		0.22 (0.03, 0.03)	0.055
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	5,075	****	****	****	****	5.52	****	-24.82	****	0.18 (0.04, 0.82)	0.027
ACEI (183-day prior, 14-day gap)	5,075	****	****	****	****	30.34	****	-24.02		0.18 (0.04, 0.82)	0.027
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	5,075	****	****	****	****	5.31	****	-27.1	****	0.16 (0.04, 0.72)	0.017
ACEI (183-day prior, 14-day gap)	5,075	****	****	****	****	32.41	****	-27.1		0.10 (0.04, 0.72)	0.017
					31 - 60 Days	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	4,098	****	****	****	****	7.33	****	-1.87	****	0.82 (0.20, 3.47)	0.791
ACEI (183-day prior, 14-day gap)	41,763	****	****	****	****	9.21	****			0.02 (0.20, 0.47)	
Fixed Ratio 1:1 Propensity Score	Matched Cond		lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	3,697	****	****	****	****	4.72	****	4.72	****	_	_
ACEI (183-day prior, 14-day gap)	3,697	****	****	****	****	0	****	7.72		_	_

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

	Number of	Person Years	Average Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!							
SV (183-day prior, 14-day gap)	4,069	****	****	****	****	7.38	****	7.38	****	_	_
ACEI (183-day prior, 14-day gap)	4,617	****	****	****	****	0	****	7.56		-	
					61 - 90 Day:	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,644	****	****	****	****	0	****	0.51	****		
ACEI (183-day prior, 14-day gap)	27,857	****	****	****	****	9.51	****	-9.51			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,646	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	1,646	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	2,629	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	3,190	****	****	****	****	0	****	0		-	
				9	91 - 180 Day	/s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,067	****	****	****	****	0	****	г эг	****		
ACEI (183-day prior, 14-day gap)	22,987	****	****	****	****	5.25	****	-5.25		-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,055	****	****	****	****	0	****	-6.84	****		
ACEI (183-day prior, 14-day gap)	1,055	****	****	****	****	6.84	****	-0.84		-	-

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

Medical Product Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	Number of New Users Matched Unco 2,055	Person Years at Risk nditional A	Person Days at Risk	Average Person Years at Risk liper= 0.09	Number of Events 5	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
ACEI (183-day prior, 14-day gap)	2,606	****	****	****	****	4.46	****	-4.46		-	-
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,282	****	****	****	****	0	****	-4.42	****	_	_
ACEI (183-day prior, 14-day gap)	12,534	****	****	****	****	4.42	****	-4.42			
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	358	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	358	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	1,276	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	1,388	****	****	****	****	0	****	0		_	
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	910	****	****	****	****	4.91	****	-0.56	****	0.91 (0.12, 7.11)	0.926
ACEI (183-day prior, 14-day gap)	8,409	****	****	****	****	5.47	****	0.50		0.51 (0.12, 7.11)	0.320
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	173	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	173	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!							
SV (183-day prior, 14-day gap)	905	****	****	****	****	4.93	****	-5.63	****	0.48 (0.04, 5.33)	0.553
ACEI (183-day prior, 14-day gap)	896	****	****	****	****	10.57	****	-5.05		0.40 (0.04, 3.33)	0.555

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Age Group: 55-64					Overell						
Site-Adjusted Analysis					Overall						
SV (183-day prior, 14-day gap)	11,494	****	****	****	****	2.62	****				
ACEI (183-day prior, 14-day gap)	97,244	****	****	****	****	8.94	****	-6.32	****	0.29 (0.15, 0.54)	<0.001
Fixed Ratio 1:1 Propensity Score	•	litional Ana	lysis: Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	11,435	****	****	****	****	3.76	****				
ACEI (183-day prior, 14-day gap)	11,435	****	****	****	****	11.74	****	-7.98	****	0.32 (0.14, 0.71)	0.005
Fixed Ratio 1:1 Propensity Score		nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	11,435	****	****	****	****	2.63	****	-5.81	****	0.30 (0.15, 0.61)	<0.001
ACEI (183-day prior, 14-day gap)	11,435	****	****	****	****	8.44	****	-5.61		0.30 (0.13, 0.01)	<u> </u>
					0 - 30 Days						
Site-Adjusted Analysis		de de de de de	****	****	to the state of		de de de de de				
SV (183-day prior, 14-day gap)	11,494	****			****	2.38	****	-14.94	****	0.14 (0.03, 0.55)	0.005
ACEI (183-day prior, 14-day gap)	97,244		****	*****	****	17.32	****				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	11,435	****	****	****	****	2.48	****	-19.85	****	0.11 (0.03, 0.48)	0.003
ACEI (183-day prior, 14-day gap)	11,435		*****			22.33	****				
Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	11,435	****	naiysis; ca	*****	****	2.4	****				
ACEI (183-day prior, 14-day gap)	11,435	****	****	****	****	2. 4 19.86	****	-17.47	****	0.12 (0.03, 0.51)	0.004
ACLI (183-day prior, 14-day gap)	11,433				31 - 60 Day						
Site-Adjusted Analysis					<u> </u>	-					
SV (183-day prior, 14-day gap)	8,991	****	****	****	****	6.63	****		****	0.05 / 0.04 . 0.40	0.70
ACEI (183-day prior, 14-day gap)	89,848	****	****	****	****	7.74	****	-1.11	<u>ጥ ጥ ጥ ጥ</u>	0.86 (0.31, 2.40)	0.78
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	8,175	****	****	****	****	8.35	****	4.19	****	2.00 / 0.27 10.02\	0.422
ACEI (183-day prior, 14-day gap)	8,175	****	****	****	****	4.18	****	4.18	,	2.00 (0.37, 10.92)	0.423

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

	Number of	Person Years	Average Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco			•							
SV (183-day prior, 14-day gap)	8,947	****	****	****	****	6.66	****	1.19	****	1.21 (0.30, 4.83)	0.791
ACEI (183-day prior, 14-day gap)	10,478	****	****	****	****	5.47	****	1.13		1.21 (0.30, 4.83)	0.751
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	5,921	****	****	****	****	4.56	****	-2.77	****	0.62/0.15 2.64\	0.532
ACEI (183-day prior, 14-day gap)	62,798	****	****	****	****	7.33	****	-2.77		0.63 (0.15, 2.64)	0.532
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	3,863	****	****	****	****	3.76	****	7.52	****	0.22 (0.02	0.341
ACEI (183-day prior, 14-day gap)	3,863	****	****	****	****	11.28	****	-7.52		0.33 (0.03, 3.20)	0.341
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	5,890	****	****	****	****	4.59	****	г ос	****	0.44/0.00 3.10)	0.210
ACEI (183-day prior, 14-day gap)	7,492	****	****	****	****	10.54	****	-5.96		0.44 (0.09, 2.19)	0.318
				9	91 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	4,693	****	****	****	****	0	****	6.20	****		_
ACEI (183-day prior, 14-day gap)	52,858	****	****	****	****	6.39	****	-6.39			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,597	****	****	****	****	0	****	2.75	****		
ACEI (183-day prior, 14-day gap)	2,597	****	****	****	****	2.75	****	-2.75	and the state of	-	-

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

Medical Product Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	Number of New Users Matched Unco 4,666	Person Years at Risk nditional A *****	Average Person Days at Risk nalysis; Ca	Average Person Years at Risk liper= 0.0!	Number of Events 5	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years		Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
ACEI (183-day prior, 14-day gap)	6,324	****	****	****	****	4.48	****	-4.48	****	-	-
71 7 7617	,			1	81 - 270 Day	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,889	****	****	****	****	1.68	****	-4.87	****	0.26 (0.04, 1.88)	0.182
ACEI (183-day prior, 14-day gap)	29,789	****	****	****	****	6.55	****	-4.67		0.20 (0.04, 1.88)	0.102
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	857	****	****	****	****	0	****	-6.89	****		
ACEI (183-day prior, 14-day gap)	857	****	****	****	****	6.89	****	-0.69		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!							
SV (183-day prior, 14-day gap)	2,875	****	****	****	****	1.68	****	-4.1	****	0.29 (0.03, 2.61)	0.27
ACEI (183-day prior, 14-day gap)	3,516	****	****	****	****	5.79	****	-4.1		0.23 (0.03, 2.01)	0.27
				2	71 - 365 Day	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,036	****	****	****	****	2.25	****	-4.07	****	0.35 (0.05, 2.60)	0.307
ACEI (183-day prior, 14-day gap)	20,218	****	****	****	****	6.32	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond										
SV (183-day prior, 14-day gap)	407	****	****	****	****	13.8	****	13.8	****	_	_
ACEI (183-day prior, 14-day gap)	407	****	****	****	****	0	****	13.0			
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	2,028	****	****	****	****	2.26	****	0.2	****	0.96 (0.06, 15.62)	0.98
ACEI (183-day prior, 14-day gap)	2,286	****	****	****	****	2.06	****	0.2		0.50 (0.00, 15.02)	0.50

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Age Group: 65+					Overall						
Site-Adjusted Analysis					Overall						
SV (183-day prior, 14-day gap)	50,618	****	****	****	****	2	****				
ACEI (183-day prior, 14-day gap)	530.994	****	****	****	****	6.03	****	-4.03	****	0.32 (0.23, 0.44)	<0.001
Fixed Ratio 1:1 Propensity Score		ditional Ana	lvsis: Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	50,470	****	****	****	****	2.2	****		****		
ACEI (183-day prior, 14-day gap)	50,470	****	****	****	****	7.76	****	-5.56	****	0.28 (0.18, 0.45)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	50,470	****	****	****	****	2.01	****	-3.06	****	0.38 (0.26, 0.55)	<0.001
ACEI (183-day prior, 14-day gap)	50,470	****	****	****	****	5.07	****	-5.06		0.36 (0.20, 0.33)	<0.001
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	50,618	****	****	****	****	3.72	****	-10.45	****	0.26 (0.15, 0.44)	<0.001
ACEI (183-day prior, 14-day gap)	530,994	****	****	****	****	14.17	****			0.20 (0.23) 0.11)	
Fixed Ratio 1:1 Propensity Score	Matched Cond										
SV (183-day prior, 14-day gap)	50,470	****	****	****	****	3.59	****	-11.32	****	0.24 (0.13, 0.44)	< 0.001
ACEI (183-day prior, 14-day gap)	50,470	****	****	****	****	14.91	****			0.21 (0.20) 0.11)	
Fixed Ratio 1:1 Propensity Score		onditional A	nalysis; Ca ****	•	****		****				
SV (183-day prior, 14-day gap)	50,470	****	****	****	****	3.73	****	-10.03	****	0.27 (0.15, 0.48)	< 0.001
ACEI (183-day prior, 14-day gap)	50,470	****	****			13.76	****				
Cita Adiusted Analysis					31 - 60 Day	S					
Site-Adjusted Analysis SV (183-day prior, 14-day gap)	40,811	****	****	****	****	1.79	****				
ACEI (183-day prior, 14-day gap)	486,760	****	****	****	****	5.4	****	-3.6	****	0.33 (0.14, 0.81)	0.015
Fixed Ratio 1:1 Propensity Score	•		lycic, Calin			J. 4					
SV (183-day prior, 14-day gap)	37,246	*****	****	*****	****	2.21	****				
ACEI (183-day prior, 14-day gap)	37,246	****	****	****	****	4.86	****	-2.65	****	0.45 (0.16, 1.31)	0.144

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

	Number of	Person Years	Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score			-	-							
SV (183-day prior, 14-day gap)	40,696	****	****	****	****	1.8	****	-3.65	****	0.33 (0.12, 0.88)	0.027
ACEI (183-day prior, 14-day gap)	46,185	****	****	****	****	5.45	****	5.05		0.55 (0.12, 0.00)	0.027
					61 - 90 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	27,874	****	****	****	****	2.4	****	2.77	****	0.47/0.10 1.14	0.003
ACEI (183-day prior, 14-day gap)	359,705	****	****	****	****	5.18	****	-2.77		0.47 (0.19, 1.14)	0.093
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	19,364	****	****	****	****	1.47	****	-1.47	****	0.50 (0.09, 2.73)	0.423
ACEI (183-day prior, 14-day gap)	19,364	****	****	****	****	2.95	****	-1.47		0.50 (0.09, 2.75)	0.425
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	27,793	****	****	****	****	2.41	****	-1.32	****	0.65 (0.22, 1.90)	0.433
ACEI (183-day prior, 14-day gap)	34,914	****	****	****	****	3.73	****	-1.52		0.05 (0.22, 1.90)	0.433
				9	91 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	22,545	****	****	****	****	0.7	****	-3.26	****	0.18 (0.06, 0.56)	0.003
ACEI (183-day prior, 14-day gap)	311,698	****	****	****	****	3.96	****	-5.20		0.18 (0.06, 0.36)	0.003
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	13,620	****	****	****	****	0	****	2.1	****		
ACEI (183-day prior, 14-day gap)	13,620	****	****	****	****	3.1	****	-3.1	and the same and the	-	-

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Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up

Medical Product Fixed Ratio 1:1 Propensity Score		Person Years at Risk Inditional A	Average Person Days at Risk nalysis; Cal	Average Person Years at Risk liper= 0.05	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	22,479	****	****	****	****	0.7 2.57	****	-1.87	****	0.27 (0.08, 0.94)	0.039
ACEI (183-day prior, 14-day gap)	30,209				81 - 270 Dav						
Site-Adjusted Analysis					01 270 Da	y 3					
SV (183-day prior, 14-day gap) ACEI (183-day prior, 14-day gap)	14,120 188,019	****	****	*****	*****	2.08 3.63	****	-1.55	****	0.57 (0.25, 1.30)	0.181
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calipe	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	4,956	****	****	****	****	2.41	****	2.44	****	0.50/0.00 3.73)	0.422
ACEI (183-day prior, 14-day gap)	4,956	****	****	****	****	4.83	****	-2.41	4444	0.50 (0.09, 2.73)	0.423
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Cal	liper= 0.05							
SV (183-day prior, 14-day gap)	14,084	****	****	****	****	2.08	****	-0.76	****	0.72 (0.26, 1.98)	0.527
ACEI (183-day prior, 14-day gap)	17,695	****	****	****	****	2.84	****	0.76		0.72 (0.20, 1.50)	0.527
				2:	71 - 365 Day	ys					
Site-Adjusted Analysis		****	di di di di di	di di di di di	****		****				
SV (183-day prior, 14-day gap)	9,854	****	****	****	****	1.38	****	-1.68	****	0.45 (0.14, 1.42)	0.173
ACEI (183-day prior, 14-day gap)	132,787				****	3.06	****				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	2,346	****	****	****	****	2.29	****	-2.29	****	0.50 (0.05, 5.51)	0.571
ACEI (183-day prior, 14-day gap)	2,346	****	****	****	****	4.59	****				
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	9,839	****	****	****	****	1.38	****	0.6	****	1.76 (0.29, 10.51)	0.537
ACEI (183-day prior, 14-day gap)	11,906	****	****	****	****	0.78	****			. , , ,	

¹Conditional analysis accounts for informative events and person-time.

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² Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 11. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Race: Unknown											
Site-Adjusted Analysis											
SV (14-day gap, history of	11,656	****	****	****	****	1.26	****				
ACEI (-183, -1))								-5.51	****	0.18 (0.07, 0.43)	< 0.001
ACEI (14-day gap)	99,645	****	****	****	****	6.77	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	11,647	****	****	****	****	1.82	****				
ACEI (-183, -1))								-7.28	****	0.20 (0.07, 0.59)	0.003
ACEI (14-day gap)	11,647	****	****	****	****	9.09	****				
Fixed Ratio 1:1 Propensity S	core Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	11,647	****	****	****	****	1.26	****				
ACEI (-183, -1))								-5.1	****	0.20 (0.08, 0.51)	< 0.001
ACEI (14-day gap)	11,647	****	****	****	****	6.36	****				
Race: American Indian											
Site-Adjusted Analysis											
SV (14-day gap, history of	242	****	****	****	****	0	****				
ACEI (-183, -1))								-2.38	****	-	-
ACEI (14-day gap)	4,525	****	****	****	****	2.38	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	234	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	234	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity S	core Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	234	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	234	****	****	****	****	0	****				

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Table 11. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number	Person	Person	Average Person	Normala	Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio (95% Confidence	Wald
Medical Product	Number of		Days at	rears at Risk	of Events	per 1,000 Person		1,000 Person	1,000 New Users	Interval) ²	P-Value ²
	New Users	Risk	Risk	RISK	or Events	Years	Users	Years	New Osers	intervaij	P-value
Race: Asian											
Site-Adjusted Analysis		****	****	****	****		****				
SV (14-day gap, history of	666	****	****	****	****	0	****	2.62	****		
ACEI (-183, -1))								-2.63	****	-	-
ACEI (14-day gap)	7,871	****	****	****	****	2.63	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	656	****	****	****	****	0	****				
ACEI (-183, -1))								-8.2	****	-	-
ACEI (14-day gap)	656	****	****	****	****	8.2	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Uncondit	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	656	****	****	****	****	0	****				
ACEI (-183, -1))								-3.98	****	-	-
ACEI (14-day gap)	656	****	****	****	****	3.98	****				
Race: Black											
Site-Adjusted Analysis											
SV (14-day gap, history of	9,015	****	****	****	****	5.6	****				
ACEI (-183, -1))	•							-16.98	****	0.24 (0.14, 0.39)	< 0.001
ACEI (14-day gap)	92,098	****	****	****	****	22.58	****			, , ,	
Fixed Ratio 1:1 Propensity So		Condition	al Analysi	s: Caliper=	: 0.05 ¹						
SV (14-day gap, history of	8,997	****	****	****	****	8.01	****				
ACEI (-183, -1))	-,							-14.02	****	0.36 (0.19, 0.70)	0.003
ACEI (14-day gap)	8,997	****	****	****	****	22.03	****			, , ,	
Fixed Ratio 1:1 Propensity So		Uncondit	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	8.997	****	****	****	****	5.62	****				
ACEI (-183, -1))	0,557					3.02		-11.34	****	0.32 (0.18, 0.56)	<0.001
ACEI (14-day gap)	8,997	****	****	****	****	16.96	****			(,)	

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Table 11. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Person		Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Pacific Islander											
Site-Adjusted Analysis											
SV (14-day gap, history of	66	****	****	****	****	53.19	****				
ACEI (-183, -1))								38.83	****	1.89 (0.19, 18.82)	0.588
ACEI (14-day gap)	741	****	****	****	****	14.36	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	59	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	59	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	59	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	59	****	****	****	****	0	****				
Race: White											
Site-Adjusted Analysis											
SV (14-day gap, history of	47,994	****	****	****	****	1.79	****				
ACEI (-183, -1))								-2.56	****	0.40 (0.28, 0.57)	< 0.001
ACEI (14-day gap)	490,002	****	****	****	****	4.35	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	47,950	****	****	****	****	1.69	****				
ACEI (-183, -1))								-4.07	****	0.29 (0.17, 0.50)	< 0.001
ACEI (14-day gap)	47,950	****	****	****	****	5.76	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	47,950	****	****	****	****	1.79	****				
ACEI (-183, -1))								-2.28	****	0.42 (0.28, 0.63)	< 0.001
ACEI (14-day gap)	47,950	****	****	****	****	4.08	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Race: Unknown											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	11,656	****	****	****	****	1.26	****	-5.51	****	0.10 (0.07 0.42)	<0.001
ACEI (183-day prior, 14-day gap)	99,645	****	****	****	****	6.77	****	-5.51		0.18 (0.07, 0.43)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	alysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	11,647	****	****	****	****	1.82	****	7.20	****	0.30 / 0.07 0.50	0.003
ACEI (183-day prior, 14-day gap)	11,647	****	****	****	****	9.09	****	-7.28	4. 4. 4. 4. 4.	0.20 (0.07, 0.59)	0.003
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	Analysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	11,647	****	****	****	****	1.26	****	-5.1	****	0.20 (0.08, 0.51)	<0.001
ACEI (183-day prior, 14-day gap)	11,647	****	****	****	****	6.36	****	-5.1		0.20 (0.08, 0.51)	<0.001
					0 - 30 Days	5					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	11,656	****	****	****	****	1.19	****	-14.8	****	0.07 (0.01, 0.51)	0.009
ACEI (183-day prior, 14-day gap)	99,645	****	****	****	****	15.99	****	-14.0		0.07 (0.01, 0.31)	0.009
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	alysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	11,647	****	****	****	****	1.24	****	12.6	****	0.09 (0.01 0.64)	0.017
ACEI (183-day prior, 14-day gap)	11,647	****	****	****	****	14.84	****	-13.6		0.08 (0.01, 0.64)	0.017
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	Analysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	11,647	****	****	****	****	1.19	****	-13	****	0.08 (0.01, 0.63)	0.016
ACEI (183-day prior, 14-day gap)	11,647	****	****	****	****	14.19	****	-13		0.00 (0.01, 0.03)	0.010
					31 - 60 Day	'S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	8,924	****	****	****	****	3.27	****	-1.79	****	0.65 (0.16, 2.72)	0.557
ACEI (183-day prior, 14-day gap)	91,186	****	****	****	****	5.05	****	-1./3		0.03 (0.10, 2.72)	0.337

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	8,088	*****	****	er= 0.05 *****	****	4.12	****				
ACEI (183-day prior, 14-day gap)	8,088	****	****	****	****	4.12	****	0	****	1.00 (0.14, 7.10)	1
Fixed Ratio 1:1 Propensity Score	,	nditional A	nalvsis: Ca	liner= 0.0	5	4.12					
SV (183-day prior, 14-day gap)	8,917	****	****	****	****	3.27	****				
ACEI (183-day prior, 14-day gap)	10,535	****	****	****	****	4.06	****	-0.79	****	0.80 (0.13, 4.82)	0.812
71021 (100 day prior) 11 day gap)	10,555				61 - 90 Days						
Site-Adjusted Analysis						-					
SV (183-day prior, 14-day gap)	6,151	****	****	****	****	2.19	****		****	/ \	
ACEI (183-day prior, 14-day gap)	64,648	****	****	****	****	5.32	****	-3.13	****	0.42 (0.06, 3.07)	0.391
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	4,017	****	****	****	****	0	****	10.00	****		
ACEI (183-day prior, 14-day gap)	4,017	****	****	****	****	10.88	****	-10.88	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	6,145	****	****	****	****	2.19	****	C F 4	****	0.25 / 0.02 .245	0.207
ACEI (183-day prior, 14-day gap)	7,599	****	****	****	****	8.73	****	-6.54		0.25 (0.03, 2.15)	0.207
				9	91 - 180 Day	rs .					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	4,905	****	****	****	****	0	****	-4.5	****	_	
ACEI (183-day prior, 14-day gap)	53,827	****	****	****	****	4.5	****	-4.5		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,674	****	****	****	****	0	****	-7.74	****		
ACEI (183-day prior, 14-day gap)	2,674	****	****	****	****	7.74	****	-7.74		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5		·				
SV (183-day prior, 14-day gap)	4,899	****	****	****	****	0	****	-4.41	****		
ACEI (183-day prior, 14-day gap)	6,304	****	****	****	****	4.41	****	-4.41		<u>-</u>	
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	3,093	****	****	****	****	0	****	-3.81	****		
ACEI (183-day prior, 14-day gap)	31,199	****	****	****	****	3.81	****	-2.01		-	_

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	950	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	950	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	3,092	****	****	****	****	0	****	-4.27	****		
ACEI (183-day prior, 14-day gap)	3,546	****	****	****	****	4.27	****	-4.27		-	-
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,169	****	****	****	****	2.09	****	-1.71	****	0.52 (0.07, 3.92)	0.528
ACEI (183-day prior, 14-day gap)	21,466	****	****	****	****	3.8	****	-1.71		0.32 (0.07, 3.32)	0.526
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	443	****	****	****	****	12.22	****	12.22	****		
ACEI (183-day prior, 14-day gap)	443	****	****	****	****	0	****	12.22	4.4.4.4.4.	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	2,168	****	****	****	****	2.09	****	2.00	****		
ACEI (183-day prior, 14-day gap)	2,331	****	****	****	****	0	****	2.09		-	-
Race: American Indian											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	242	****	****	****	****	0	****	-2.38	****		
ACEI (183-day prior, 14-day gap)	4,525	****	****	****	****	2.38	****	-2.30		-	-

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score			Person Days at Risk lysis; Calip		Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	234	****	****	****	****	0	****	0	****	-	-
ACEI (183-day prior, 14-day gap)	234	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score		nditional A	nalysis; Ca ****	•			ale ale ale ale				
SV (183-day prior, 14-day gap)	234	****	****	****	****	0	****	0	****	-	-
ACEI (183-day prior, 14-day gap)	234	****	****			0	****				
City Adings of Augustasia					0 - 30 Days						
Site-Adjusted Analysis	242	****	****	****	****		****				
SV (183-day prior, 14-day gap)	242	****	****	****	****	0	****	-5.54	****	-	-
ACEI (183-day prior, 14-day gap)	4,525				****	5.54	****				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	234	****	****	****	****	0	****	0	****	-	_
ACEI (183-day prior, 14-day gap)	234	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	234	****	****	****	****	0	****	0	****	-	_
ACEI (183-day prior, 14-day gap)	234	****	****	****	****	0	****	-			
					31 - 60 Day	S					
Site-Adjusted Analysis		****	****	****	****		****				
SV (183-day prior, 14-day gap)	187					0		0	****	-	-
ACEI (183-day prior, 14-day gap)	4,184	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	168	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	168	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	182	****	****	****	****	0	****	0	****	-	_
ACEI (183-day prior, 14-day gap)	218	****	****	****	****	0	****				
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	117	****	****	****	****	0	****	0	****	-	_
ACEI (183-day prior, 14-day gap)	2,739	****	****	****	****	0	****	•			

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	78	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	78	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	114	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	153	****	****	****	****	0	****	U		-	
				g	1 - 180 Day	rs .					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	97	****	****	****	****	0	****	-5.01	****	_	_
ACEI (183-day prior, 14-day gap)	2,252	****	****	****	****	5.01	****	5.01			
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	51	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	51	****	****	****	****	0	****	U		_	
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!							
SV (183-day prior, 14-day gap)	94	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	121	****	****	****	****	0	****			<u>-</u>	
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	54	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	1,257	****	****	****	****	0	****	3			

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	Number of New Users Matched Cond	Person Years at Risk litional Ana *****	Average Person Days at Risk lysis; Calipo	Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years		Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
ACEI (183-day prior, 14-day gap)	15	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	54	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	65	****	****	****	****	0	****	U		-	
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	36	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	837	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	****	****	****	****	****	0	****	<u> </u>			
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	37	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	47	****	****	****	****	0	****	<u> </u>			
Race: Asian											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	666	****	****	****	****	0	****	-2.63	****	_	_
ACEI (183-day prior, 14-day gap)	7,871	****	****	****	****	2.63	****	2.03			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap) ACEI (183-day prior, 14-day gap)	656 656	****	****	*****	****	0 8.2	****	-8.2	****	-	-

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Person Days at Risk		Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco		-	liper= 0.0!							
SV (183-day prior, 14-day gap)	656	****	****	****	****	0	****	-3.98	****	_	_
ACEI (183-day prior, 14-day gap)	656	****	****	****	****	3.98	****	-3.96		_	
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	666	****	****	****	****	0	****	-4.83	****		
ACEI (183-day prior, 14-day gap)	7,871	****	****	****	****	4.83	****	-4.83		-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	656	****	****	****	****	0	****	21.04	****		
ACEI (183-day prior, 14-day gap)	656	****	****	****	****	21.84	****	-21.84		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	656	****	****	****	****	0	****	10.40	****		
ACEI (183-day prior, 14-day gap)	656	****	****	****	****	19.49	****	-19.49		-	-
					31 - 60 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	507	****	****	****	****	0	****	-6.02	****		
ACEI (183-day prior, 14-day gap)	7,147	****	****	****	****	6.02	****	-0.02		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	454	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	454	****	****	****	****	0	****	0		<u> </u>	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	501	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	590	****	****	****	****	0	****	U		-	-

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	350	****	****	****	****	0	****	F 4F	****		
ACEI (183-day prior, 14-day gap)	5,095	****	****	****	****	5.15	****	-5.15	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	234	****	****	****	****	0	****		****		
ACEI (183-day prior, 14-day gap)	234	****	****	****	****	0	****	0	4.4.4.4.4	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	345	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	429	****	****	****	****	0	****	0		-	-
				9	91 - 180 Day	/s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	266	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	4,335	****	****	****	****	0	****	U			
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	147	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	147	****	****	****	****	0	****	U			
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	264	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	362	****	****	****	****	0	****	U			
	_			1	81 - 270 Da	ys		_			
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	176	****	****	****	****	0	****	0	****	_	
ACEI (183-day prior, 14-day gap)	2,368	****	****	****	****	0	****	U		-	_

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score	Number of New Users Matched Cond		Average Person Days at Risk lysis; Calipe	Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	56	*****	****	****	****	0	****	0	****	-	-
ACEI (183-day prior, 14-day gap)	56					0	****				
Fixed Ratio 1:1 Propensity Score		nditional A	nalysis; Ca	!iper= 0.0! ****	****		****				
SV (183-day prior, 14-day gap)	177	****	****	****	****	0	****	0	****	-	-
ACEI (183-day prior, 14-day gap)	202	****	****			0	****				
Site Adjusted Applysis					71 - 365 Da	ys					
Site-Adjusted Analysis	124	****	****	****	****	0	****				
SV (183-day prior, 14-day gap) ACEI (183-day prior, 14-day gap)	1.546	****	****	****	****	0	****	0	****	-	-
	,	J:4: I A	leader Cellin	0 0F ¹							
Fixed Ratio 1:1 Propensity Score		****	iysis; Calipo	er= 0.05	****		****				
SV (183-day prior, 14-day gap)	26	****	****	****	****	0	****	0	****	-	-
ACEI (183-day prior, 14-day gap)	26					0	****				
Fixed Ratio 1:1 Propensity Score		****	naiysis; ca	*****	****		****				
SV (183-day prior, 14-day gap)	128	****	****	****	****	0	****	0	****	-	-
ACEI (183-day prior, 14-day gap)	127	****	****	****	****	0	****				
Race: Black					0						
Site-Adjusted Analysis					Overall						
	0.015	****	****	****	****	5.6	****				
SV (183-day prior, 14-day gap)	9,015	****	****	****	****		****	-16.98	****	0.24 (0.14, 0.39)	< 0.001
ACEI (183-day prior, 14-day gap)	92,098					22.58					
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	8,997	****	****	****	****	8.01	****	-14.02	****	0.36 (0.19, 0.70)	0.003
ACEI (183-day prior, 14-day gap)	8,997	****	****	****	****	22.03	****			(,	

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

			Average	Average		Incidence Rate per	Risk per	Incidence Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	• ′	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score						rears	USEIS	reison reals	New Osers	iiiteivaij	r-value
SV (183-day prior, 14-day gap)	8,997	****	****	*****	****	5.62	****				
ACEI (183-day prior, 14-day gap)	8,997 8,997	****	****	****	****	16.96	****	-11.34	****	0.32 (0.18, 0.56)	< 0.001
ACLI (183-day prior, 14-day gap)	8,997				0 - 30 Days						
Site-Adjusted Analysis					O SO Days						
SV (183-day prior, 14-day gap)	9,015	****	****	****	****	12.05	****				
ACEI (183-day prior, 14-day gap)	92,098	****	****	****	****	48.75	****	-36.7	****	0.24 (0.12, 0.49)	<0.001
Fixed Ratio 1:1 Propensity Score		itional Ana	lysis: Caling	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	8,997	****	****	****	****	12.49	****				
ACEI (183-day prior, 14-day gap)	8.997	****	****	****	****	42.15	****	-29.66	****	0.30 (0.13, 0.65)	0.003
Fixed Ratio 1:1 Propensity Score		nditional A	nalvsis: Ca	liper= 0.05	5	72.13					
SV (183-day prior, 14-day gap)	8,997	****	****	****	****	12.07	****				
ACEI (183-day prior, 14-day gap)	8,997	****	****	****	****	40.64	****	-28.57	****	0.30 (0.13, 0.65)	0.002
(200 00) [2100]	5,551			3	31 - 60 Days						
Site-Adjusted Analysis					•						
SV (183-day prior, 14-day gap)	7,146	****	****	****	****	10.79	****	7.10	****	0.50 / 0.24 4.46\	0.257
ACEI (183-day prior, 14-day gap)	84,673	****	****	****	****	17.98	****	-7.19	****	0.59 (0.24, 1.46)	0.257
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	6,522	****	****	****	****	11	****	2.75	****	4 22 / 0 20	0.706
ACEI (183-day prior, 14-day gap)	6,522	****	****	****	****	8.25	****	2.75	יוי יוי יוי יוי	1.33 (0.30, 5.96)	0.706
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	7,131	****	****	****	****	10.82	****	1.65	****	0.96 (0.37 3.70)	0.702
ACEI (183-day prior, 14-day gap)	8,247	****	****	****	****	12.47	****	-1.65		0.86 (0.27, 2.70)	0.792

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	4,325	****	****	****	****	0	****	-18.68	****	_	_
ACEI (183-day prior, 14-day gap)	56,518	****	****	****	****	18.68	****	10.00			
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,673	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	2,673	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	4,312	****	****	****	****	0	****	-9.48	****		
ACEI (183-day prior, 14-day gap)	5,589	****	****	****	****	9.48	****	-9.46		-	
				9	1 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	3,268	****	****	****	****	1.69	****	-12.92	****	0.12 (0.02, 0.83)	0.032
ACEI (183-day prior, 14-day gap)	47,205	****	****	****	****	14.6	****	-12.92		0.12 (0.02, 0.83)	0.032
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,643	****	****	****	****	0	****	4.00	****		
ACEI (183-day prior, 14-day gap)	1,643	****	****	****	****	4.82	****	-4.82		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	3,254	****	****	****	****	1.69	****	-12.76	****	0.11 (0.01, 0.88)	0.037
ACEI (183-day prior, 14-day gap)	4,644	****	****	****	****	14.45	****	-12.76		0.11 (0.01, 0.88)	0.037
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,852	****	****	****	****	2.69	****	-9.47	****	0.22 (0.03, 1.58)	0.131
ACEI (183-day prior, 14-day gap)	24,182	****	****	****	****	12.16	****	-J.4 <i>1</i>		0.22 (0.03, 1.36)	0.131

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score	Number of New Users Matched Cond	Person Years at Risk litional Ana	Average Person Days at Risk	Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	485	****	****	****	****	0	****	26.5	****		
ACEI (183-day prior, 14-day gap)	485	****	****	****	****	26.5	****	-26.5	4 4 4 4	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	1,845	****	****	****	****	2.7	****	-4.24	****	0.39 (0.04, 3.74)	0.413
ACEI (183-day prior, 14-day gap)	2,323	****	****	****	****	6.94	****	-4.24		0.39 (0.04, 3.74)	0.413
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,245	****	****	****	****	0	****	-11.59	****	_	_
ACEI (183-day prior, 14-day gap)	15,670	****	****	****	****	11.59	****	-11.55			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	192	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	192	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	1,240	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	1,386	****	****	****	****	0	****	U		-	
Race: Pacific Islander											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	66	****	****	****	****	53.19	****	38.83	****	1.89 (0.19, 18.82)	0.588
ACEI (183-day prior, 14-day gap)	741	****	****	****	****	14.36	****	36.63		1.05 (0.15, 10.02)	0.566
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	59	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	59	****	****	****	****	0	****	0		-	-

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score	Number of New Users Matched Unco	Person Years at Risk nditional A	Average Person Days at Risk nalysis; Ca	Average Person Years at Risk liper= 0.0	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	59	****	****	****	****	0	****	0	****	_	
ACEI (183-day prior, 14-day gap)	59	****	****	****	****	0	****				
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	66	****	****	****	****	0	****	-34.75	****	_	_
ACEI (183-day prior, 14-day gap)	741	****	****	****	****	34.75	****	34.73			
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	59	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	59	****	****	****	****	0	****	U		_	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	59	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	59	****	****	****	****	0	****	0			
					31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	52	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	654	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	42	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	42	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	49	****	****	****	****	0	****	0	****	_	
ACEI (183-day prior, 14-day gap)	49	****	****	****	****	0	****	U		_	-

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk		Number of Events 61 - 90 Day	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Site-Adjusted Analysis					or so bay	3					
SV (183-day prior, 14-day gap)	35	****	****	****	****	383.14	****	256.7	****	7.05 / 0.20 4.64 4)	0.402
ACEI (183-day prior, 14-day gap)	496	****	****	****	****	26.44	****	356.7	4 4 4 4	7.85 (0.38, 161.1)	0.182
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	22	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	22	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	32	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	41	****	****	****	****	0	****	U		-	
				9	91 - 180 Day	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	28	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	424	****	****	****	****	0	****	<u> </u>			
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	15	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	15	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	26	****	****	****	****	0	****	0	****		
ACEI (183-day prior, 14-day gap)	32	****	****	****	****	0	****	U		-	
				1	.81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	15	****	****	****	****	0	****	-24.5	****	_	_
ACEI (183-day prior, 14-day gap)	208	****	****	****	****	24.5	****	-24.5		-	-

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score	Number of New Users Matched Cond	Person Years at Risk litional Ana	Average Person Days at Risk lysis; Calipe	Average Person Years at Risk er= 0.05 ¹	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****	_	
ACEI (183-day prior, 14-day gap)	****	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	16	****	****	****	****	0	****	0	****	-	_
ACEI (183-day prior, 14-day gap)	17	****	****	****	****	0	****	-			
				2	71 - 365 Da	ys					
Site-Adjusted Analysis	****	****	****	****	****		****				
SV (183-day prior, 14-day gap)		****	****	****	****	0	****	0	****	-	-
ACEI (183-day prior, 14-day gap)	138				****	0	****				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	****	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score				-							
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****	_	_
ACEI (183-day prior, 14-day gap)	12	****	****	****	****	0	****				
Race: White											
					Overall						
Site-Adjusted Analysis		de de de de de	de de de de de	4.4.4.4.4	de de de de de		de de de de de				
SV (183-day prior, 14-day gap)	47,994	****	****	****	****	1.79	****	-2.56	****	0.40 (0.28, 0.57)	< 0.001
ACEI (183-day prior, 14-day gap)	490,002	****	****	****	****	4.35	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond		-								
SV (183-day prior, 14-day gap)	47,950	****	****	****	****	1.69	****	-4.07	****	0.29 (0.17, 0.50)	< 0.001
ACEI (183-day prior, 14-day gap)	47,950	****	****	****	****	5.76	****	4.07		0.23 (0.17, 0.30)	\0.001

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score		Person Years at Risk Inditional A	Average Person Days at Risk nalysis; Ca	Average Person Years at Risk liper= 0.05	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	47,950 47,050	****	****	****	****	1.79	****	-2.28	****	0.42 (0.28, 0.63)	<0.001
ACEI (183-day prior, 14-day gap)	47,950				0 - 30 Days	4.08					
Site-Adjusted Analysis					0 - 30 Days)					
SV (183-day prior, 14-day gap) ACEI (183-day prior, 14-day gap)	47,994 490,002	****	****	****	*****	2.52 9.17	*****	-6.66	****	0.27 (0.14, 0.53)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	47,950	****	****	****	****	2.6	****	-8.97	****	0.33 / 0.11 0.46	<0.001
ACEI (183-day prior, 14-day gap)	47,950	****	****	****	****	11.57	****	-8.97		0.23 (0.11, 0.46)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	47,950	****	****	****	****	2.52	****	-8.79	****	0.22 (0.11, 0.45)	<0.001
ACEI (183-day prior, 14-day gap)	47,950	****	****	****	****	11.3	****	-0.75		0.22 (0.11, 0.43)	\0.001
					31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	38,981	****	****	****	****	1.88	****	-2.29	****	0.45 (0.19, 1.11)	0.083
ACEI (183-day prior, 14-day gap)	450,526	****	****	****	****	4.17	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calipo	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	35,736	****	****	****	****	1.84	****	-1.84	****	0.50 (0.15, 1.66)	0.258
ACEI (183-day prior, 14-day gap)	35,736	****	****	****	****	3.68	****	1.07		0.50 (0.15, 1.00)	0.230
Fixed Ratio 1:1 Propensity Score	Matched Unco			•							
SV (183-day prior, 14-day gap)	38,945	****	****	****	****	1.88	****	-1.62	****	0.53 (0.19, 1.53)	0.243
ACEI (183-day prior, 14-day gap)	43,997	****	****	****	****	3.5	****	1.02		0.55 (0.15, 1.55)	0.243

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	26,678	****	****	****	****	2.51	****	-1.24	****	0.67 (0.27, 1.64)	0.379
ACEI (183-day prior, 14-day gap)	333,484	****	****	****	****	3.74	****	-1.24		0.07 (0.27, 1.04)	0.373
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	18,611	****	****	****	****	2.29	****	0.76	****	0.75 / 0.17 2.25\	0.706
ACEI (183-day prior, 14-day gap)	18,611	****	****	****	****	3.06	****	-0.76		0.75 (0.17, 3.35)	0.706
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	26,652	****	****	****	****	2.51	****	0.63	****	0.90 (0.36 . 3.46)	0.702
ACEI (183-day prior, 14-day gap)	33,227	****	****	****	****	3.13	****	-0.63		0.80 (0.26, 2.46)	0.702
				9	1 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	21,709	****	****	****	****	0.48	****	-2.44	****	0.17 (0.04, 0.67)	0.012
ACEI (183-day prior, 14-day gap)	289,671	****	****	****	****	2.93	****	-2.44		0.17 (0.04, 0.07)	0.012
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	13,175	****	****	****	****	0	****	1.06	****		
ACEI (183-day prior, 14-day gap)	13,175	****	****	****	****	1.06	****	-1.06		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	21,689	****	****	****	****	0.48	****	1 24	****	0.39 / 0.06 1.30)	0.103
ACEI (183-day prior, 14-day gap)	28,845	****	****	****	****	1.73	****	-1.24		0.28 (0.06, 1.30)	0.103
				18	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	13,664	****	****	****	****	2.14	****	-1.05	****	0.67 (0.29, 1.52)	0.339
ACEI (183-day prior, 14-day gap)	176,322	****	****	****	****	3.19	****	-1.03		0.07 (0.29, 1.32)	0.339

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Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time

	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Rate per 1,000 Person Years	Risk per 1,000 New Users	Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score M	latched Condi	itional Anal	lysis; Calipe	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	4,841	****	****	****	****	1.24	****	-2.48	****	0.33 (0.03, 3.20)	0.341
ACEI (183-day prior, 14-day gap)	4,841	****	****	****	****	3.72	****	-2.46		0.33 (0.03, 3.20)	0.541
Fixed Ratio 1:1 Propensity Score M	latched Unco	nditional A	nalysis; Cal	liper= 0.05	5						
SV (183-day prior, 14-day gap)	13,654	****	****	****	****	2.14	****	-0.5	****	0.80 (0.28, 2.23)	0.664
ACEI (183-day prior, 14-day gap)	17,028	****	****	****	****	2.65	****	-0.5		0.00 (0.20, 2.23)	0.004
				2	71 - 365 Day	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	9,601	****	****	****	****	1.88	****	-0.71	****	0.72 (0.26, 1.98)	0.53
ACEI (183-day prior, 14-day gap)	125,105	****	****	****	****	2.59	****	-0.71		0.72 (0.20, 1.30)	0.55
Fixed Ratio 1:1 Propensity Score M	latched Condi	itional Anal	lysis; Calipe	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,298	****	****	****	****	0	****	2.20	****		
ACEI (183-day prior, 14-day gap)	2,298	****	****	****	****	2.29	****	-2.29	THE THE THE THE	-	-
Fixed Ratio 1:1 Propensity Score M	latched Unco	nditional A	nalysis; Cal	liper= 0.05	5						
SV (183-day prior, 14-day gap)	9,595	****	****	****	****	1.88	****	0.20	****	1 16 (0 20 4 62)	0.927
ACEI (183-day prior, 14-day gap)	11,538	****	****	****	****	1.6	****	0.28		1.16 (0.29, 4.63)	0.837

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

	Number of	Years at	Person	Person	Number	per 1,000 Person	1,000	Difference per	in Risk per	(95% Confidence	Wald
Medical Product	New Users	Risk	Days at	Years at	of Events	Years	New	1,000 Person	1,000	Interval)	P-Value
Site-Adjusted Analysis											
SV (14-day gap, history of	49,140	****	****	****	****	2.55	****				
ARBs (-183, -1))								-0.47	****	0.80 (0.58, 1.09)	0.161
ARBs (14-day gap)	337,083	****	****	****	****	3.02	****				
Fixed Ratio 1:1 Propensity Se	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	49,137	****	****	****	****	3.3	****				
ARBs (-183, -1))								-0.1	****	0.97 (0.61, 1.56)	0.904
ARBs (14-day gap)	49,137	****	****	****	****	3.4	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	49,137	****	****	****	****	2.55	****				
ARBs (-183, -1))								-0.31	****	0.85 (0.58, 1.26)	0.417
ARBs (14-day gap)	49,137	****	****	****	****	2.85	****				
Propensity Score Adjusted S	tratified Analy	ysis; Perce	ntiles= 10	1							
SV (14-day gap, history of	49,140	****	****	****	****	2.55	****				
ARBs (-183, -1))								-0.47	****	0.94 (0.68, 1.29)	0.685
ARBs (14-day gap)	337,083	****	****	****	****	3.02	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 14. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	49,140	****	****	****	****	2.55	****	-0.47	****	0.80 (0.58, 1.09)	0.161
ARBs (183-day prior, 14-day gap)	337,083	****	****	****	****	3.02	****	-0.47		0.80 (0.38, 1.03)	0.101
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	49,137	****	****	****	****	3.3	****	0.1	****	0.07/0.61 1.56\	0.004
ARBs (183-day prior, 14-day gap)	49,137	****	****	****	****	3.4	****	-0.1		0.97 (0.61, 1.56)	0.904
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	49,137	****	****	****	****	2.55	****	-0.31	****	0.85 (0.58, 1.26)	0.417
ARBs (183-day prior, 14-day gap)	49,137	****	****	****	****	2.85	****	-0.51		0.85 (0.38, 1.20)	0.417
					0 - 30 Days	;					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	49,140	****	****	****	****	3.86	****	-2.1	****	0.64 (0.37, 1.10)	0.104
ARBs (183-day prior, 14-day gap)	337,083	****	****	****	****	5.96	****	-2.1		0.04 (0.37, 1.10)	0.104
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	49,137	****	****	****	****	3.69	****	1 42	****	0.73 / 0.35 1.47\	0.271
ARBs (183-day prior, 14-day gap)	49,137	****	****	****	****	5.1	****	-1.42		0.72 (0.35, 1.47)	0.371
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	49,137	****	****	****	****	3.86	****	-1.74	****	0.68 (0.35, 1.33)	0.259
ARBs (183-day prior, 14-day gap)	49,137	****	****	****	****	5.61	****	-1.74		0.08 (0.33, 1.33)	0.239
					31 - 60 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	39,111	****	****	****	****	3.01	****	-0.41	****	0.89 (0.43, 1.84)	0.748
ARBs (183-day prior, 14-day gap)	316,224	****	****	****	****	3.42	****	-0.41		0.03 (0.43, 1.04)	0.740

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Table 14. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score				er= 0.05 ¹							
SV (183-day prior, 14-day gap)	36,512	****	****	****	****	3.57	****	-1.34	****	0.73 (0.29, 1.81)	0.493
ARBs (183-day prior, 14-day gap)	36,512	****	****	****	****	4.91	****			0.75 (0.25) 1.01)	0.155
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	39,110	****	****	****	****	3.01	****	-1.49	****	0.67 (0.28, 1.58)	0.362
ARBs (183-day prior, 14-day gap)	45,890	****	****	****	****	4.5	****	21.13		0.07 (0.20, 2.30)	
					61 - 90 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	26,476	****	****	****	****	3.55	****	0.74	****	1.30 (0.59, 2.86)	0.513
ARBs (183-day prior, 14-day gap)	243,445	****	****	****	****	2.81	****	0.74		1.30 (0.33, 2.00)	0.515
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	19,243	****	****	****	****	2.97	****	2.07	****		
ARBs (183-day prior, 14-day gap)	19,243	****	****	****	****	0	****	2.97		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	26,476	****	****	****	****	3.55	****	2.55	****		
ARBs (183-day prior, 14-day gap)	35,682	****	****	****	****	0	****	3.55		-	-
				9	1 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	21,374	****	****	****	****	2.23	****	0.02	****	0.00/0.50 1.06)	0.066
ARBs (183-day prior, 14-day gap)	214,230	****	****	****	****	2.25	****	-0.02		0.99 (0.50, 1.96)	0.966
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	13,557	****	****	****	****	2.61	****	_	****		
ARBs (183-day prior, 14-day gap)	13,557	****	****	****	****	2.61	****	0	****	1.00 (0.29, 3.45)	1
Fixed Ratio 1:1 Propensity Score		nditional A	nalvsis: Ca	liper= 0.0!	5	=: • =					
SV (183-day prior, 14-day gap)	21,374	****	****	****	****	2.23	****		****		
ARBs (183-day prior, 14-day gap)	31,191	****	****	****	****	2.84	****	-0.61	****	0.78 (0.34, 1.77)	0.552
, , , , , , , , , , , , , , , , , , , ,	,			1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	13,101	****	****	****	****	1.13	****	0.01	****	0.56/0.47 4.75	0.224
ARBs (183-day prior, 14-day gap)	130,069	****	****	****	****	2.07	****	-0.94	~ ~ * * *	0.56 (0.17, 1.78)	0.324

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Table 14. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

		Person	Average Person	Average Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score I	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	4,935	****	****	****	****	3.62	****	2.41	****	3.00 (0.31, 28.84)	0.341
ARBs (183-day prior, 14-day gap)	4,935	****	****	****	****	1.21	****	2.41		3.00 (0.31, 28.64)	0.541
Fixed Ratio 1:1 Propensity Score I	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	13,101	****	****	****	****	1.13	****	-0.22	****	0.84 (0.20, 3.54)	0.817
ARBs (183-day prior, 14-day gap)	18,451	****	****	****	****	1.35	****	-0.22		0.84 (0.20, 3.34)	0.017
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	8,995	****	****	****	****	1.02	****	-0.53	****	0.68 (0.16, 2.82)	0.592
ARBs (183-day prior, 14-day gap)	92,640	****	****	****	****	1.56	****	-0.55		0.00 (0.10, 2.02)	0.552
Fixed Ratio 1:1 Propensity Score I	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,357	****	****	****	****	2.26	****	2.26	****		
ARBs (183-day prior, 14-day gap)	2,357	****	****	****	****	0	****	2.26		-	-
Fixed Ratio 1:1 Propensity Score I	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	8,995	****	****	****	****	1.02	****	-0.79	****	0.59 (0.11 2.02)	0.521
ARBs (183-day prior, 14-day gap)	12,667	****	****	****	****	1.81	****	-0.79		0.58 (0.11, 3.02)	0.321

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 15. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)

	Number of	Person	Average Person	Average Person	Number	Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	Wald
Medical Product		Years at	Days at	Years at		per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	
No Angioedema (-183, -1)	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
Site-Adjusted Analysis											
SV (14-day gap, history of	49,082	****	****	****	****	2.19	****				
, , , , , ,	49,062					2.19		-0.24	****	0.87 (0.62, 1.22)	0.421
ARBs (-183, -1))	336,258	****	****	****	****	2.43	****	-0.24		0.87 (0.02, 1.22)	0.421
ARBs (14-day gap)		Canadistan	al Arabia	a. Calinan	0.051	2.43					
Fixed Ratio 1:1 Propensity So		****	****	*****	*****	2.02	****				
SV (14-day gap, history of	49,079	****	****	***	****	2.82	****	0.10	****	1 07 / 0 (4 1 01)	0.700
ARBs (-183, -1))	40.070	****	****	****	****	2.52	****	0.19		1.07 (0.64, 1.81)	0.789
ARBs (14-day gap)	49,079					2.62	****				
Fixed Ratio 1:1 Propensity So		****	enal Analy	ysis; Calipe	*****		****				
SV (14-day gap, history of	49,079	****	****	****	****	2.19	****	0.05	****	0.07 (0.57 . 4.00)	0.504
ARBs (-183, -1))								-0.25	****	0.87 (0.57, 1.32)	0.501
ARBs (14-day gap)	49,079	****	****	****	****	2.45	****				
Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	58	****	****	****	****	333.15	****				
ARBs (-183, -1))								61.51	****	1.13 (0.49, 2.58)	0.778
ARBs (14-day gap)	825	****	****	****	****	271.63	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.051						
SV (14-day gap, history of	55	****	****	****	****	304.57	****				
ARBs (-183, -1))								-203.05	****	0.60 (0.14, 2.51)	0.484
ARBs (14-day gap)	55	****	****	****	****	507.61	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	55	****	****	****	****	296.21	****				
ARBs (-183, -1))								13.27	****	0.76 (0.21, 2.70)	0.672
ARBs (14-day gap)	55	****	****	****	****	282.94	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time

	Number of	Person Years	Average Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	•	Interval) ²	P-Value ²
No Angioedema (-183, -1)											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	49,082	****	****	****	****	2.19	****	-0.24	****	0.87 (0.62, 1.22)	0.421
ARBs (183-day prior,14-day gap)	336,258	****	****	****	****	2.43	****	-0.24		0.87 (0.02, 1.22)	0.421
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	49,079	****	****	****	****	2.82	****	0.19	****	1.07 (0.64, 1.81)	0.789
ARBs (183-day prior,14-day gap)	49,079	****	****	****	****	2.62	****	0.19		1.07 (0.04, 1.01)	0.769
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	49,079	****	****	****	****	2.19	****	-0.25	****	0.87 (0.57, 1.32)	0.501
ARBs (183-day prior,14-day gap)	49,079	****	****	****	****	2.45	****	-0.23		0.87 (0.37, 1.32)	0.301
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	49,082	****	****	****	****	2.49	****	-1.6	****	0.60 (0.31, 1.19)	0.146
ARBs (183-day prior,14-day gap)	336,258	****	****	****	****	4.08	****	1.0		0.00 (0.01, 1.13)	0.140
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	49,079	****	****	****	****	2.27	****	-1.13	****	0.67 (0.27, 1.63)	0.374
ARBs (183-day prior,14-day gap)	49,079	****	****	****	****	3.4	****	-1.13		0.07 (0.27, 1.03)	0.374
Fixed Ratio 1:1 Propensity Score	Matched Unco			liper= 0.0							
SV (183-day prior, 14-day gap)	49,079	****	****	****	****	2.49	****	-1.6	****	0.61 (0.27, 1.37)	0.229
ARBs (183-day prior,14-day gap)	49,079	****	****	****	****	4.08	****	1.0		0.01 (0.27, 1.37)	0.223
					31 - 60 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	39,070	****	****	****	****	3.01	****	0.02	****	1.01 (0.49, 2.11)	0.969
ARBs (183-day prior,14-day gap)	315,501	****	****	****	****	2.99	****			(-:, -:)	
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	36,476	****	****	****	****	3.58	****	-1.34	****	0.73 (0.29, 1.81)	0.493
ARBs (183-day prior,14-day gap)	36,476	****	****	****	****	4.92	****	-1.54		0.73 (0.23, 1.81)	0.455

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time

	Number of	Person Years	Average Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco			liper= 0.0!							
SV (183-day prior, 14-day gap)	39,069	****	****	****	****	3.01	****	-1.5	****	0.67 (0.28, 1.58)	0.362
ARBs (183-day prior,14-day gap)	45,840	****	****	****	****	4.51	****	-1.5		0.67 (0.26, 1.36)	0.302
				(61 - 90 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	26,448	****	****	****	****	3.05	****	0.02	****	1 42 (0 60 2 22)	0.424
ARBs (183-day prior,14-day gap)	242,928	****	****	****	****	2.23	****	0.82		1.42 (0.60, 3.33)	0.424
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	19,220	****	****	****	****	2.97	****	2.07	****		
ARBs (183-day prior,14-day gap)	19,220	****	****	****	****	0	****	2.97		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	26,448	****	****	****	****	3.05	****	2.05	****		
ARBs (183-day prior,14-day gap)	35,641	****	****	****	****	0	****	3.05		-	
				9	1 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	21,350	****	****	****	****	2.24	****	0.24	****	1 11 / 0 [6 2 22]	0.750
ARBs (183-day prior,14-day gap)	213,786	****	****	****	****	2	****	0.24		1.11 (0.56, 2.22)	0.759
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	13,539	****	****	****	****	2.61	****	0.53	****	1 35 / 0 34 / 4 55\	0.720
ARBs (183-day prior,14-day gap)	13,539	****	****	****	****	2.09	****	0.52	and the state of	1.25 (0.34, 4.65)	0.739

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score		Person Years at Risk onditional A	Average Person Days at Risk Inalysis; Ca	Average Person Years at Risk liper= 0.0	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	21,350	****	****	****	****	2.24	****	-0.43	****	0.83 (0.36, 1.90)	0.663
ARBs (183-day prior,14-day gap)	31,152	****	****			2.67	****				
Site-Adjusted Analysis				1	81 - 270 Da	ys					
SV (183-day prior, 14-day gap)	13,089	****	****	****	****	1.13	****				
ARBs (183-day prior,14-day gap)	129,786	****	****	****	****	1.15	****	-0.72	****	0.62 (0.19, 2.00)	0.425
			hada Calla	o or ¹		1.03					
Fixed Ratio 1:1 Propensity Score		****	iysis; Calip	er= 0.05 ****	****	2.62	****				
SV (183-day prior, 14-day gap)	4,924	****	****	****	****	3.63	****	3.63	****	-	-
ARBs (183-day prior,14-day gap)	4,924					0	****				
Fixed Ratio 1:1 Propensity Score			nalysis; Ca	*****			****				
SV (183-day prior, 14-day gap)	13,089	****			****	1.13		0.05	****	1.05 (0.24, 4.72)	0.946
ARBs (183-day prior,14-day gap)	18,422	****	****	****	****	1.08	****				
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	8,986	****	****	****	****	1.02	****	-0.39	****	0.75 (0.18, 3.13)	0.69
ARBs (183-day prior,14-day gap)	92,446	****	****	****	****	1.41	****			0.75 (0.10, 0.10,	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,353	****	****	****	****	2.26	****	2.26	****		
ARBs (183-day prior,14-day gap)	2,353	****	****	****	****	0	****	2.26			
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	8,986	****	****	****	****	1.02	****	0.42	****	0.71 / 0.12 2.00\	0.604
ARBs (183-day prior,14-day gap)	12,645	****	****	****	****	1.45	****	-0.43		0.71 (0.13, 3.88)	0.694

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time

		Person	Average Person	Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio (95% Confidence	Wald
A A a disa di Dura da sat	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	•	
Medical Product Angioedema (-183, -1)	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Aligioedellia (-165, -1)					Overall						
Site-Adjusted Analysis					Overall						
SV (183-day prior, 14-day gap)	58	****	****	****	****	333.15	****				
ARBs (183-day prior,14-day gap)	825	****	****	****	****	271.63	****	61.51	****	1.13 (0.49, 2.58)	0.778
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lvsis: Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	55	****	****	****	****	304.57	****	202.05	****	0.60 (0.44 - 2.54)	0.404
ARBs (183-day prior,14-day gap)	55	****	****	****	****	507.61	****	-203.05	****	0.60 (0.14, 2.51)	0.484
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	55	****	****	****	****	296.21	****	13.27	****	0.76 (0.21, 2.70)	0.672
ARBs (183-day prior,14-day gap)	55	****	****	****	****	282.94	****	15.27		0.70 (0.21, 2.70)	0.072
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	58	****	****	****	****	1,295.34	****	491.05	****	1.51 (0.60, 3.80)	0.378
ARBs (183-day prior,14-day gap)	825	****	****	****	****	804.29	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond		lysis; Calip								
SV (183-day prior, 14-day gap)	55	****	****	****	****	847.46	****	-282.49	****	0.75 (0.17, 3.35)	0.706
ARBs (183-day prior,14-day gap)	55	****	****	****	****	1,129.94	****	202.43		0.73 (0.17, 3.33)	0.700
Fixed Ratio 1:1 Propensity Score			-	-							
SV (183-day prior, 14-day gap)	55	****	****	****	****	1,061.01	****	110.89	****	1.07 (0.27, 4.30)	0.919
ARBs (183-day prior,14-day gap)	55	****	****	****	****	950.12	****			- (- , ,	
City Adiabat Analysis					31 - 60 Day	S					
Site-Adjusted Analysis	41	****	****	****	****	0	****				
SV (183-day prior, 14-day gap)	41 725	****	****	****	****	•	****	-194.97	****	-	-
ARBs (183-day prior,14-day gap)	725					194.97					
Fixed Ratio 1:1 Propensity Score		itional Ana	lysis; Calip	er= 0.05 ⁻	****		****				
SV (183-day prior, 14-day gap)	36	****	****	****	****	0	****	-390.63	****	-	-
ARBs (183-day prior,14-day gap)	36	***	T T T T T	ጥጥጥ	ጥጥጥጥ	390.63	ጥጥጥጥ				

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	39	****	****	****	****	0	****	-262.47	****		
ARBs (183-day prior,14-day gap)	50	****	****	****	****	262.47	****	-202.47		-	-
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	28	****	****	****	****	460.83	****	184.79	****	1 52 / 0 20 11 70	0.69
ARBs (183-day prior,14-day gap)	522	****	****	****	****	276.04	****	104.79		1.52 (0.20, 11.78)	0.09
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	22	****	****	****	****	0	****	0	****		
ARBs (183-day prior,14-day gap)	22	****	****	****	****	0	****	0		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	29	****	****	****	****	432.9	****	432.9	****	_	
ARBs (183-day prior,14-day gap)	42	****	****	****	****	0	****	432.9			
				9	91 - 180 Day	rs					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	24	****	****	****	****	0	****	-118.47	****	_	_
ARBs (183-day prior,14-day gap)	449	****	****	****	****	118.47	****	-110.47			_
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	21	****	****	****	****	0	****	0	****		
ARBs (183-day prior,14-day gap)	21	****	****	****	****	0	****	U		-	-

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	26	Person Years at Risk Inditional A	Average Person Days at Risk nalysis; Ca	Average Person Years at Risk liper= 0.0! *****	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
ARBs (183-day prior,14-day gap)	36	****	****			145.56	*****				
Site-Adjusted Analysis				1	81 - 270 Da	ys					
SV (183-day prior, 14-day gap) ARBs (183-day prior,14-day gap)	13 286	****	****	****	****	0 106.48	****	-106.48	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lvsis: Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap) ARBs (183-day prior,14-day gap)	****	****	****	*****	****	0 0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score			•	•							
SV (183-day prior, 14-day gap) ARBs (183-day prior,14-day gap)	16 23	*****	****	****	*****	0 0	****	0	****	-	-
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap) ARBs (183-day prior,14-day gap)	**** 197	*****	*****	****	****	0 66.89	****	-66.89	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap) ARBs (183-day prior,14-day gap)	*****	****	****	****	*****	0 0	****	0	****	-	
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!	5		_	_		_	
SV (183-day prior, 14-day gap) ARBs (183-day prior,14-day gap)	11 17	****	****	****	*****	0 243.31	****	-243.31	****	-	-

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 17. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	Interval)	P-Value
No Angioedema (ever, -1)	Treat Obers	T.I.S.K	- THISK	111011	0. 200	10015	U 3013	10015	Hell Coers	e.rui,	Tuluc
Site-Adjusted Analysis											
SV (14-day gap, history of	48,390	****	****	****	****	1.92	****				
ARBs (-183, -1))								-0.11	****	0.91 (0.63, 1.32)	0.627
ARBs (14-day gap)	329,726	****	****	****	****	2.03	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	48,383	****	****	****	****	2.47	****				
ARBs (-183, -1))								0.49	****	1.25 (0.69, 2.25)	0.457
ARBs (14-day gap)	48,383	****	****	****	****	1.97	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	48,383	****	****	****	****	1.92	****				
ARBs (-183, -1))								-0.02	****	0.96 (0.60, 1.51)	0.845
ARBs (14-day gap)	48,383	****	****	****	****	1.94	****				
Angioedema (ever, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	750	****	****	****	****	45.4	****				
ARBs (-183, -1))								-2.55	****	0.83 (0.45, 1.54)	0.558
ARBs (14-day gap)	7,357	****	****	****	****	47.94	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	744	****	****	****	****	64.88	****				_
ARBs (-183, -1))								12.98	****	1.25 (0.49, 3.17)	0.638
ARBs (14-day gap)	744	****	****	****	****	51.9	****				
Fixed Ratio 1:1 Propensity So	core Matched		onal Anal		er= 0.05						
SV (14-day gap, history of	744	****	****	****	****	41.87	****				
ARBs (-183, -1))								9.65	****	1.16 (0.49, 2.74)	0.739
ARBs (14-day gap)	744	****	****	****	****	32.22	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 18. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies

	Number of	Person Years at	Average Person Days at	Person	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
No Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	42,674	****	****	****	****	2.28	****				
ARBs (-183, -1))								-0.3	****	0.84 (0.59, 1.20)	0.332
ARBs (14-day gap)	282,648	****	****	****	****	2.59	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	42,666	****	****	****	****	2.76	****				
ARBs (-183, -1))								0	****	1.00 (0.57, 1.74)	1
ARBs (14-day gap)	42,666	****	****	****	****	2.76	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	42,666	****	****	****	****	2.28	****				
ARBs (-183, -1))								-0.21	****	0.88 (0.57, 1.37)	0.57
ARBs (14-day gap)	42,666	****	****	****	****	2.49	****				
Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	6,466	****	****	****	****	4.48	****				
ARBs (-183, -1))								-1.01	****	0.76 (0.39, 1.50)	0.427
ARBs (14-day gap)	54,435	****	****	****	****	5.5	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	6,436	****	****	****	****	4.22	****				
ARBs (-183, -1))								-0.84	****	0.83 (0.25, 2.73)	0.763
ARBs (14-day gap)	6,436	****	****	****	****	5.06	****				
Fixed Ratio 1:1 Propensity So	core Matched										
SV (14-day gap, history of	6,436	****	****	****	****	4.51	****				
ARBs (-183, -1))								1.05	****	1.25 (0.49, 3.15)	0.64
ARBs (14-day gap)	6,436	****	****	****	****	3.46	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



	, , , , , , , , , , , , , , , , , , ,			Average		•	Risk per	Incidence	Difference	Hazard Ratio	
		Person	Person	Person	Number	Incidence	1,000	Rate	in Risk per	(95%	
	Number of	Years	Days	Years	of	Rate per 1,000	New	Difference	1,000	Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	per 1,000	New Users	Interval) ²	P-Value ²
Sex: Male											
					Overall						
Site-Adjusted Analysis											
SV (14-day gap, history of	29,914	****	****	****	****	1.92	****				
ARBs (-183, -1))								-0.98	****	0.63 (0.40, 1.00)	0.05
ARBs (14-day gap)	149,212	****	****	****	****	2.9	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	29,883	****	****	****	****	2.72	****				
ARBs (-183, -1))								-0.32	****	0.89 (0.47, 1.72)	0.739
ARBs (14-day gap)	29,883	****	****	****	****	3.04	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Uncor	nditional An	alysis; Calip	per= 0.05							
SV (14-day gap, history of	29,883	****	****	****	****	1.92	****				
ARBs (-183, -1))								-0.81	****	0.67 (0.39, 1.16)	0.154
ARBs (14-day gap)	29,883	****	****	****	****	2.73	****				
					0 - 30 Day	S					
Site-Adjusted Analysis											
SV (14-day gap, history of	29,914	****	****	****	****	4.07	****				
ARBs (-183, -1))								-0.96	****	0.79 (0.39, 1.58)	0.501
ARBs (14-day gap)	149,212	****	****	****	****	5.02	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Analy	/sis; Caliper	'= 0.05 ¹							
SV (14-day gap, history of	29,883	****	****	****	****	4.19	****				
ARBs (-183, -1))								0	****	1.00 (0.40, 2.52)	1
ARBs (14-day gap)	29,883	****	****	****	****	4.19	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Uncor										
SV (14-day gap, history of	29,883	****	****	****	****	4.07	****				
ARBs (-183, -1))								-0.13	****	0.96 (0.39, 2.35)	0.922
ARBs (14-day gap)	29,883	****	****	****	****	4.2	****				

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				Average		,	Risk per	Incidence	Difference	Hazard Ratio	
		Person	Person	Person	Number	Incidence	1,000	Rate	in Risk per	(95%	
	Number of	Years	Days	Years	of	Rate per 1,000	New	Difference	1,000	Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	per 1,000	New Users	Interval) ²	P-Value ²
					31 - 60 Day	/s					
Site-Adjusted Analysis											
SV (14-day gap, history of	23,979	****	****	****	****	1.22	****				
ARBs (-183, -1))								-1.66	****	0.42 (0.10, 1.77)	0.239
ARBs (14-day gap)	139,746	****	****	****	****	2.88	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Analy	ysis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	22,255	****	****	****	****	1.46	****				
ARBs (-183, -1))								-2.2	****	0.40 (0.08, 2.06)	0.273
ARBs (14-day gap)	22,255	****	****	****	****	3.66	****				
Fixed Ratio 1:1 Propensity Sco	ore Matched Unco	nditional An	nalysis; Cali _l	per= 0.05							
SV (14-day gap, history of	23,959	****	****	****	****	1.22	****				
ARBs (-183, -1))								-2.75	****	0.31 (0.07, 1.47)	0.142
ARBs (14-day gap)	27,741	****	****	****	****	3.97	****				
					61 - 90 Day	/S					
Site-Adjusted Analysis											
SV (14-day gap, history of	16,323	****	****	****	****	3.29	****				
ARBs (-183, -1))								0.88	****	1.42 (0.48, 4.15)	0.526
ARBs (14-day gap)	107,317	****	****	****	****	2.41	****				
Fixed Ratio 1:1 Propensity Sco	ore Matched Condi										
SV (14-day gap, history of	11,742	****	****	****	****	2.44	****				
ARBs (-183, -1))								2.44	****	-	-
ARBs (14-day gap)	11,742	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sco	ore Matched Uncor		nalysis; Cali _l	per= 0.05							
SV (14-day gap, history of	16,314	****	****	****	****	3.29	****				
ARBs (-183, -1))								3.29	****	-	-
ARBs (14-day gap)	21,548	****	****	****	****	0	****				

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	<u>-</u>		Average	Average			Risk per	Incidence	Difference	Hazard Ratio	
		Person	Person	Person	Number	Incidence	1,000	Rate	in Risk per	(95%	
	Number of	Years	Days	Years	of	Rate per 1,000	New	Difference	1,000	Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	per 1,000	New Users	Interval) ²	P-Value ²
				g)1 - 180 Da	ys					
Site-Adjusted Analysis											
SV (14-day gap, history of	13,186	****	****	****	****	1.61	****				
ARBs (-183, -1))								-1.16	****	0.57 (0.20, 1.57)	0.275
ARBs (14-day gap)	94,188	****	****	****	****	2.77	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	8,232	****	****	****	****	2.61	****				
ARBs (-183, -1))								-0.87	****	0.75 (0.17, 3.35)	0.706
ARBs (14-day gap)	8,232	****	****	****	****	3.47	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	13,178	****	****	****	****	1.61	****				
ARBs (-183, -1))								-2.28	****	0.40 (0.13, 1.23)	0.11
ARBs (14-day gap)	18,720	****	****	****	****	3.89	****				
				1	81 - 270 Da	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	8,155	****	****	****	****	0.6	****				
ARBs (-183, -1))								-1.23	****	0.34 (0.05, 2.55)	0.296
ARBs (14-day gap)	56,397	****	****	****	****	1.83	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	2,967	****	****	****	****	2	****				
ARBs (-183, -1))								0	****	1.00 (0.06, 15.99)	1
ARBs (14-day gap)	2,967	****	****	****	****	2	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	8,149	****	****	****	****	0.6	****				
ARBs (-183, -1))								-0.77	****	0.42 (0.04, 4.08)	0.458
ARBs (14-day gap)	10,875	****	****	****	****	1.38	****				

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Distributed Database (3DD) be	, , , , , , , , , , , , , , , , , , , ,			Average		,	Risk per	Incidence	Difference	Hazard Ratio	
		Person	Person	Person	Number	Incidence	1,000	Rate	in Risk per	(95%	
	Number of	Years	Days	Years	of	Rate per 1,000	New	Difference	1,000	Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	per 1,000	New Users	Interval) ²	P-Value ²
				2	71 - 365 Da	iys					
Site-Adjusted Analysis											
SV (14-day gap, history of	5,618	****	****	****	****	0	****				
ARBs (-183, -1))								-2.15	****	-	-
ARBs (14-day gap)	39,949	****	****	****	****	2.15	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Analy	ysis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	1,428	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	1,428	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Unco	nditional An	alysis; Calip	er= 0.05							
SV (14-day gap, history of	5,616	****	****	****	****	0	****				
ARBs (-183, -1))								-1.24	****	-	-
ARBs (14-day gap)	7,452	****	****	****	****	1.24	****				
Sex: Female											
					Overall						
Site-Adjusted Analysis											
SV (14-day gap, history of	19,226	****	****	****	****	3.56	****				
ARBs (-183, -1))								0.45	****	1.07 (0.70, 1.64	0.749
ARBs (14-day gap)	187,871	****	****	****	****	3.11	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Analy	ysis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	19,218	****	****	****	****	4.52	****				
ARBs (-183, -1))								0.25	****	1.06 (0.55, 2.05	0.866
ARBs (14-day gap)	19,218	****	****	****	****	4.27	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Unco	nditional An	alysis; Calip	per= 0.05							
SV (14-day gap, history of	19,218	****	****	****	****	3.56	****				
ARBs (-183, -1))								0.88	****	1.27 (0.71, 2.27	0.413
ARBs (14-day gap)	19,218	****	****	****	****	2.68	****				

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	•		Average	Average		•	Risk per	Incidence	Difference	Hazard Ratio	
		Person	Person	Person	Number	Incidence	1,000	Rate	in Risk per	(95%	
	Number of	Years	Days	Years	of	Rate per 1,000	New	Difference	1,000	Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	per 1,000	New Users	Interval) ²	P-Value ²
					0 - 30 Day	S					
Site-Adjusted Analysis											
SV (14-day gap, history of	19,226	****	****	****	****	3.54	****				
ARBs (-183, -1))								-3.17	****	0.52 (0.21, 1.28)	0.156
ARBs (14-day gap)	187,871	****	****	****	****	6.71	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	itional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	19,218	****	****	****	****	2.91	****				
ARBs (-183, -1))								-3.64	****	0.44 (0.14, 1.44)	0.177
ARBs (14-day gap)	19,218	****	****	****	****	6.55	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	19,218	****	****	****	****	3.54	****				
ARBs (-183, -1))								-2.97	****	0.54 (0.18, 1.57)	0.256
ARBs (14-day gap)	19,218	****	****	****	****	6.51	****				
					31 - 60 Day	/s					
Site-Adjusted Analysis											
SV (14-day gap, history of	15,132	****	****	****	****	5.85	****				
ARBs (-183, -1))								2.01	****	1.53 (0.65, 3.57)	0.328
ARBs (14-day gap)	176,478	****	****	****	****	3.84	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	itional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	14,102	****	****	****	****	7	****				
ARBs (-183, -1))								1.17	****	1.20 (0.37, 3.93)	0.763
ARBs (14-day gap)	14,102	****	****	****	****	5.83	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	15,128	****	****	****	****	5.86	****				
ARBs (-183, -1))								1.22	****	1.26 (0.41, 3.91)	0.688
ARBs (14-day gap)	17,918	****	****	****	****	4.63	****				

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	•		Average	Average		•	Risk per	Incidence	Difference	Hazard Ratio	
		Person	Person	Person	Number	Incidence	1,000	Rate	in Risk per	(95%	
	Number of	Years	Days	Years	of	Rate per 1,000	New	Difference	1,000	Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	per 1,000	New Users	Interval) ²	P-Value ²
					61 - 90 Day	/s					
Site-Adjusted Analysis											
SV (14-day gap, history of	10,153	****	****	****	****	3.97	****				
ARBs (-183, -1))								0.85	****	1.31 (0.40, 4.26)	0.658
ARBs (14-day gap)	136,128	****	****	****	****	3.13	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	itional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	7,322	****	****	****	****	5.83	****				
ARBs (-183, -1))								5.83	****	-	-
ARBs (14-day gap)	7,322	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional An	alysis; Calip	oer= 0.05							
SV (14-day gap, history of	10,151	****	****	****	****	3.97	****				
ARBs (-183, -1))								3.97	****	-	-
ARBs (14-day gap)	13,812	****	****	****	****	0	****				
				g	91 - 180 Da	ys					
Site-Adjusted Analysis											
SV (14-day gap, history of	8,188	****	****	****	****	3.25	****				
ARBs (-183, -1))								1.39	****	1.78 (0.70, 4.52)	0.222
ARBs (14-day gap)	120,042	****	****	****	****	1.86	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	itional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	5,187	****	****	****	****	4.04	****				
ARBs (-183, -1))								1.35	****	1.50 (0.25, 8.98)	0.657
ARBs (14-day gap)	5,187	****	****	****	****	2.69	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional An	alysis; Cali	oer= 0.05							
SV (14-day gap, history of	8,186	****	****	****	****	3.25	****				
ARBs (-183, -1))								1.88	****	2.34 (0.56, 9.82)	0.244
ARBs (14-day gap)	12,064	****	****	****	****	1.37	****				

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			Average	Average			Risk per	Incidence	Difference	Hazard Ratio	
		Person	Person	Person	Number	Incidence	1,000	Rate	in Risk per	(95%	
	Number of	Years	Days	Years	of	Rate per 1,000	New	Difference	1,000	Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	per 1,000	New Users	Interval) ²	P-Value ²
				1	81 - 270 Da	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	4,946	****	****	****	****	2	****				
ARBs (-183, -1))								-0.25	****	0.90 (0.22, 3.76)	0.887
ARBs (14-day gap)	73,672	****	****	****	****	2.25	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi	itional Analy	/sis; Calipe	= 0.05 ¹							
SV (14-day gap, history of	1,909	****	****	****	****	3.11	****				
ARBs (-183, -1))								0	****	1.00 (0.06, 15.99)	1
ARBs (14-day gap)	1,909	****	****	****	****	3.11	****				
Fixed Ratio 1:1 Propensity Score	e Matched Unco	nditional An	alysis; Cali _l	per= 0.05							
SV (14-day gap, history of	4,945	****	****	****	****	2	****				
ARBs (-183, -1))								0.61	****	1.53 (0.22, 10.90)	0.67
ARBs (14-day gap)	7,169	****	****	****	****	1.39	****				
				2	71 - 365 Da	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	3,377	****	****	****	****	2.73	****				
ARBs (-183, -1))								1.62	****	2.69 (0.61, 11.92)	0.194
ARBs (14-day gap)	52,691	****	****	****	****	1.11	****				
Fixed Ratio 1:1 Propensity Score	e Matched Condi	itional Analy	/sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	920	****	****	****	****	5.82	****				
ARBs (-183, -1))								5.82	****	-	-
ARBs (14-day gap)	920	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	e Matched Unco	nditional An	alysis; Cali _l	per= 0.05							
SV (14-day gap, history of	3,377	****	****	****	****	2.72	****				
ARBs (-183, -1))								0.87	****	1.58 (0.22, 11.22)	0.649
ARBs (14-day gap)	4,919	****	****	****	****	1.86	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 20. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

			Average	Average			Risk per	Incidence Rate	Difference		
		Person	Person	Person		Incidence Rate	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at	Number	per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
Age Group: 18-44 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	1,164	****	****	****	****	0	****				
ARBs (-183, -1))								-7.89	****	-	-
ARBs (14-day gap)	8,502	****	****	****	****	7.89	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	1,154	****	****	****	****	0	****				
ARBs (-183, -1))								-5.39	****	-	-
ARBs (14-day gap)	1,154	****	****	****	****	5.39	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	1,154	****	****	****	****	0	****				
ARBs (-183, -1))								-2.66	****	-	-
ARBs (14-day gap)	1,154	****	****	****	****	2.66	****				
Age Group: 45-54 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	2,653	****	****	****	****	3.55	****				
ARBs (-183, -1))								-0.77	****	0.86 (0.26, 2.82)	0.799
ARBs (14-day gap)	18,293	****	****	****	****	4.32	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	2,641	****	****	****	****	4.24	****				
ARBs (-183, -1))								-4.24	****	0.50 (0.09, 2.73)	0.423
ARBs (14-day gap)	2,641	****	****	****	****	8.49	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	2,641	****	****	****	****	3.56	****				_
ARBs (-183, -1))								-2.53	****	0.61 (0.15, 2.42)	0.479
ARBs (14-day gap)	2,641	****	****	****	****	6.09	****				

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Table 20. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person	Number of Events	Incidence Rate per 1,000 Person	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence	Wald
Age Group: 55-64 Years	New Osers	RISK	RISK	RISK	or Events	Years	users	rears	New Osers	Interval)	P-Value
Site-Adjusted Analysis											
SV (14-day gap, history of	5,990	****	****	****	****	5.14	****				
ARBs (-183, -1))	3,330					5.14		1.14	****	1.25 (0.64, 2.45)	0.506
ARBs (14-day gap)	40,547	****	****	****	****	4	****			(0.0 ., ,	0.000
Fixed Ratio 1:1 Propensity S		Condition	al Analysi	s· Caliner=	0.051						
SV (14-day gap, history of	5,945	****	****	*****	****	7.18	****				
ARBs (-183, -1))	3,343					7.10		3.59	****	2.00 (0.60, 6.64)	0.258
ARBs (14-day gap)	5.945	****	****	****	****	3.59	****	0.00		(0.00, 0.0 .)	0.200
Fixed Ratio 1:1 Propensity S	- /	Unconditi	ional Anal	ysis; Calipo	er= 0.05	0.00					
SV (14-day gap, history of	5,945	****	****	****	****	5.17	****				
ARBs (-183, -1))								3.47	****	2.89 (0.91, 9.25)	0.073
ARBs (14-day gap)	5,945	****	****	****	****	1.69	****				
Age Group: 65+ Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	39,333	****	****	****	****	2.18	****				
ARBs (-183, -1))								-0.52	****	0.76 (0.52, 1.10)	0.146
ARBs (14-day gap)	269,741	****	****	****	****	2.71	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	39,269	****	****	****	****	2.94	****				
ARBs (-183, -1))								0	****	1.00 (0.57, 1.74)	1
ARBs (14-day gap)	39,269	****	****	****	****	2.94	****				
Fixed Ratio 1:1 Propensity S	core Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	39,269	****	****	****	****	2.19	****				
ARBs (-183, -1))								-0.47	****	0.78 (0.49, 1.23)	0.29
ARBs (14-day gap)	39,269	****	****	****	****	2.65	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

		Person	Average Person	Average Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	• •	Interval) ²	P-Value ²
Age Group: 18-44											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,164	****	****	****	****	0	****	-7.89	****		
ARBs (183-day prior, 14-day gap)	8,502	****	****	****	****	7.89	****	-7.89		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,154	****	****	****	****	0	****	F 20	****		
ARBs (183-day prior, 14-day gap)	1,154	****	****	****	****	5.39	****	-5.39		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	1,154	****	****	****	****	0	****	-2.66	****	_	
ARBs (183-day prior, 14-day gap)	1,154	****	****	****	****	2.66	****	-2.00			
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,164	****	****	****	****	0	****	-5.9	****	_	_
ARBs (183-day prior, 14-day gap)	8,502	****	****	****	****	5.9	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,154	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	1,154	****	****	****	****	0	****	0			
Fixed Ratio 1:1 Propensity Score	Matched Unco			liper= 0.0!							
SV (183-day prior, 14-day gap)	1,154	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	1,154	****	****	****	****	0	****				_
					31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	904	****	****	****	****	0	****	-7.65	****	-	_
ARBs (183-day prior, 14-day gap)	7,923	****	****	****	****	7.65	****				

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score		****	iysis; Calipo	er= 0.05	****		****				
SV (183-day prior, 14-day gap)	811	****	****	****	****	0	****	-21.5	****	-	-
ARBs (183-day prior, 14-day gap)	811					21.5	****				
Fixed Ratio 1:1 Propensity Score		nditional A	naiysis; Ca	*****	****		****				
SV (183-day prior, 14-day gap)	899	****	****	****	****	0	****	-14.46	****	-	-
ARBs (183-day prior, 14-day gap)	1,034	****	****			14.46	*****				
Cita Adiustad Analysis					61 - 90 Day	S					
Site-Adjusted Analysis	F70	****	****	****	****		****				
SV (183-day prior, 14-day gap)	570	****	****	****	****	0	****	-5.33	****	-	-
ARBs (183-day prior, 14-day gap)	5,003				4-4-4-4-4	5.33	4, 4, 4, 4, 4				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	327	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	327	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	567	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	654	****	****	****	****	0	****				
				9	1 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	446	****	****	****	****	0	****	-16.53	****	_	_
ARBs (183-day prior, 14-day gap)	4,048	****	****	****	****	16.53	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond		lysis; Calipo								
SV (183-day prior, 14-day gap)	197	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	197	****	****	****	****	0	****	0		_	
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	•	5						
SV (183-day prior, 14-day gap)	446	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	499	****	****	****	****	0	****	0		_	
				18	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	264	****	****	****	****	0	****	-5.1	****	_	_
ARBs (183-day prior, 14-day gap)	1,994	****	****	****	****	5.1	****	-3.1		-	-

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score					OI EVEITES	TCUIS	03013	Terson rears	New Oscis	intervary	1 Value
SV (183-day prior, 14-day gap)	58	****	****	****	****	0	****				
ARBs (183-day prior, 14-day gap)	58	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score		onditional A	Analysis: Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	267	****	****	****	****	0	****		****		
ARBs (183-day prior, 14-day gap)	256	****	****	****	****	0	****	0	****	-	-
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	192	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	1,316	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	33	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	33	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	Analysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	193	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	170	****	****	****	****	0	****	0		-	-
Age Group: 45-54											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,653	****	****	****	****	3.55	****	-0.77	****	0.86 (0.26, 2.82)	0.799
ARBs (183-day prior, 14-day gap)	18,293	****	****	****	****	4.32	****	-0.77		0.00 (0.20, 2.82)	0.799

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,641	****	****	****	****	4.24	****	-4.24	****	0.50 (0.09, 2.73)	0.423
ARBs (183-day prior, 14-day gap)	2,641	****	****	****	****	8.49	****	-4.24		0.30 (0.09, 2.73)	0.423
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	2,641	****	****	****	****	3.56	****	-2.53	****	0.61 (0.15, 2.42)	0.479
ARBs (183-day prior, 14-day gap)	2,641	****	****	****	****	6.09	****	-2.55		0.61 (0.15, 2.42)	0.479
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,653	****	****	****	****	0	****	-10.27	****		
ARBs (183-day prior, 14-day gap)	18,293	****	****	****	****	10.27	****	-10.27		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,641	****	****	****	****	0	****	10.70	****		
ARBs (183-day prior, 14-day gap)	2,641	****	****	****	****	10.78	****	-10.78	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	2,641	****	****	****	****	0	****	0.53	****		
ARBs (183-day prior, 14-day gap)	2,641	****	****	****	****	9.53	****	-9.53	****	-	-
					31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,051	****	****	****	****	0	****	-4.29	****		
ARBs (183-day prior, 14-day gap)	17,081	****	****	****	****	4.29	****	-4.29		-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,882	****	****	****	****	0	****	10.05	****		
ARBs (183-day prior, 14-day gap)	1,882	****	****	****	****	18.36	****	-18.36	****	-	-
Fixed Ratio 1:1 Propensity Score		nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	2,042	****	****	****	****	0	****	44.06	****		
ARBs (183-day prior, 14-day gap)	2,436	****	****	****	****	11.86	****	-11.86	4.4.4.4.4	-	-
					61 - 90 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,326	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	11,640	****	****	****	****	0	****	0		-	-

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

			Average	Average		Incidence Rate per	Risk per	Incidence Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	•	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹						•	
SV (183-day prior, 14-day gap)	848	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	848	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0							
SV (183-day prior, 14-day gap)	1,321	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	1,705	****	****	****	****	0	****				
				Ş	91 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,040	****	****	****	****	10.1	****	6.5	****	2.90 (0.58, 14.51)	0.196
ARBs (183-day prior, 14-day gap)	9,733	****	****	****	****	3.6	****	0.5		2.30 (0.36, 14.31)	0.130
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	549	****	****	****	****	13.32	****	12.22	****		
ARBs (183-day prior, 14-day gap)	549	****	****	****	****	0	****	13.32		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	1,039	****	****	****	****	10.11	****	5.88	****	2.46 (0.22, 27.20)	0.463
ARBs (183-day prior, 14-day gap)	1,398	****	****	****	****	4.23	****	3.00		2.46 (0.22, 27.20)	0.403
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	637	****	****	****	****	7.75	****	5.81	****	4.09 (0.36, 46.23)	0.255
ARBs (183-day prior, 14-day gap)	5,198	****	****	****	****	1.94	****	5.01		7.03 (0.30, 40.23)	0.233

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	184	*****	****	*****	****	31.69	****				
ARBs (183-day prior, 14-day gap)	184	****	****	****	****	0	****	31.69	****	-	-
Fixed Ratio 1:1 Propensity Score		nditional A	nalvsis: Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	638	****	****	****	****	7.74	****		****		
ARBs (183-day prior, 14-day gap)	723	****	****	****	****	0	****	7.74	****	-	-
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	435	****	****	****	****	0	****	-2.69	****	_	
ARBs (183-day prior, 14-day gap)	3,436	****	****	****	****	2.69	****	-2.03			
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	88	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	88	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	435	****	****	****	****	0	****	-9.96	****	_	_
ARBs (183-day prior, 14-day gap)	477	****	****	****	****	9.96	****	-9.90			
Age Group: 55-64											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	5,990	****	****	****	****	5.14	****	1.14	****	1.25 (0.64, 2.45)	0.506
ARBs (183-day prior, 14-day gap)	40,547	****	****	****	****	4	****			2 (3.3 .,)	
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	5,945	****	****	****	****	7.18	****	3.59	****	2.00 (0.60, 6.64)	0.258
ARBs (183-day prior, 14-day gap)	5,945	****	****	****	****	3.59	****	3.33		2.00 (0.00, 0.04)	0.230

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

			A	A		Incidence	Dialona.	Incidence	D:#*		
		_	Average	Average		Rate per	Risk per	Rate	Difference	Hazard Ratio	
		Person	Person	Person		1,000	1,000	Difference	in Risk		
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.05							
SV (183-day prior, 14-day gap)	5,945	****	****	****	****	5.17	****	3.47	****	2.89 (0.91, 9.25)	0.073
ARBs (183-day prior, 14-day gap)	5,945	****	****	****	****	1.69	****	3.47		2.69 (0.91, 9.23)	0.073
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	5,990	****	****	****	****	9.23	****	1 22	****	1.07/0.27 2.09\	0.001
ARBs (183-day prior, 14-day gap)	40,547	****	****	****	****	8.02	****	1.22		1.07 (0.37, 3.08)	0.901
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 1							
SV (183-day prior, 14-day gap)	5,945	****	****	****	****	9.61	****	4.81	****	2.00 (0.37, 10.92)	0.423
ARBs (183-day prior, 14-day gap)	5,945	****	****	****	****	4.81	****	4.01		2.00 (0.37, 10.92)	0.425
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	5,945	****	****	****	****	9.3	****	Г ОГ	****	2 10 / 0 20 11 44\	0.202
ARBs (183-day prior, 14-day gap)	5,945	****	****	****	****	4.24	****	5.05		2.10 (0.38, 11.44)	0.393
				;	31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	4,618	****	****	****	****	6.43	****	4.18	****	2.92 (0.58, 14.60)	0.193
ARBs (183-day prior, 14-day gap)	37,952	****	****	****	****	2.25	****	4.10		2.92 (0.38, 14.00)	0.193
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	4,220	****	****	****	****	8.01	****	4.01	****	2.00 (0.19, 22.06)	0.571
ARBs (183-day prior, 14-day gap)	4,220	****	****	****	****	4.01	****	4.01		2.00 (0.18, 22.06)	0.571
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5	•		_	_		
SV (183-day prior, 14-day gap)	4,594	****	****	****	****	6.47	****	3.87	****	2.34 (0.21, 25.82)	0.487
ARBs (183-day prior, 14-day gap)	5,466	****	****	****	****	2.6	****	3.87		2.54 (0.21, 25.82)	0.487

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

						Incidence		Incidence			
			Average	Average		Rate per	Risk per	Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					61 - 90 Day	'S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	3,044	****	****	****	****	8.87	****	6.48	****	3.86 (0.74, 20.09)	0.109
ARBs (183-day prior, 14-day gap)	27,412	****	****	****	****	2.39	****	0.46		3.80 (0.74, 20.03)	0.105
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,036	****	****	****	****	7.12	****	7.12	****	_	_
ARBs (183-day prior, 14-day gap)	2,036	****	****	****	****	0	****	7.12		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	3,028	****	****	****	****	8.91	****	8.91	****	_	
ARBs (183-day prior, 14-day gap)	3,974	****	****	****	****	0	****	8.91		<u>-</u>	
				9	91 - 180 Day	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,406	****	****	****	****	2.2	****	-1.19	****	0.65 (0.09, 5.00)	0.682
ARBs (183-day prior, 14-day gap)	23,326	****	****	****	****	3.39	****	1.15		0.03 (0.03, 3.00)	0.002
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,367	****	****	****	****	5.16	****	0	****	1.00 (0.06, 15.99)	1
ARBs (183-day prior, 14-day gap)	1,367	****	****	****	****	5.16	****	0		1.00 (0.00, 13.33)	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	2,394	****	****	****	****	2.21	****	0.5	****	1.15 (0.07, 18.54)	0.922
ARBs (183-day prior, 14-day gap)	3,331	****	****	****	****	1.71	****	0.5		1.13 (0.07, 18.34)	0.322
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,482	****	****	****	****	0	****	-3.39	****	_	_
ARBs (183-day prior, 14-day gap)	13,307	****	****	****	****	3.39	****	-3.39		<u>-</u>	-

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond										
SV (183-day prior, 14-day gap)	482	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	482	****	****	****	****	0	****	0		_	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	1,479	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	1,832	****	****	****	****	0	****	0		_	
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,012	****	****	****	****	4.54	****	1	****	1.57 (0.19, 12.73)	0.675
ARBs (183-day prior, 14-day gap)	9,049	****	****	****	****	3.54	****	1		1.37 (0.19, 12.73)	0.073
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	214	****	****	****	****	0	****		****		
ARBs (183-day prior, 14-day gap)	214	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	1,010	****	****	****	****	4.56	****	4.50	****		
ARBs (183-day prior, 14-day gap)	1,204	****	****	****	****	0	****	4.56	4. 4. 4. 4. 4.	-	-
Age Group: 65+											
					Overall						
Site-Adjusted Analysis										_	
SV (183-day prior, 14-day gap)	39,333	****	****	****	****	2.18	****	0.53	****	0.76 / 0.53 1.10\	0.146
ARBs (183-day prior, 14-day gap)	269,741	****	****	****	****	2.71	****	-0.52		0.76 (0.52, 1.10)	0.146
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	39,269	****	****	****	****	2.94	****		****	4.00/057.473	
ARBs (183-day prior, 14-day gap)	39,269	****	****	****	****	2.94	****	0	ተተተተ	1.00 (0.57, 1.74)	1

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

						Incidence		Incidence			
			Average	Average		Rate per	Risk per	Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	39,269	****	****	****	****	2.19	****	-0.47	****	0.78 (0.49, 1.23)	0.29
ARBs (183-day prior, 14-day gap)	39,269	****	****	****	****	2.65	****	-0.47		0.76 (0.49, 1.25)	0.29
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	39,333	****	****	****	****	3.43	****	-1.93	****	0.63 (0.33, 1.20)	0.161
ARBs (183-day prior, 14-day gap)	269,741	****	****	****	****	5.37	****	-1.93		0.03 (0.33, 1.20)	0.101
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	39,269	****	****	****	****	3.18	****	1 77	****	0.64 / 0.39 1.40	0.201
ARBs (183-day prior, 14-day gap)	39,269	****	****	****	****	4.95	****	-1.77		0.64 (0.28, 1.49)	0.301
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	39,269	****	****	****	****	3.44	****	-1.99	****	0.63 (0.29, 1.38)	0.246
ARBs (183-day prior, 14-day gap)	39,269	****	****	****	****	5.42	****	-1.99		0.03 (0.29, 1.36)	0.246
				;	31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	31,540	****	****	****	****	2.78	****	-0.62	****	0.82 (0.35, 1.89)	0.639
ARBs (183-day prior, 14-day gap)	253,270	****	****	****	****	3.41	****	-0.02		0.02 (0.33, 1.83)	0.033
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	29,335	****	****	****	****	3.29	****	-0.55	****	0.86 (0.29, 2.55)	0.782
ARBs (183-day prior, 14-day gap)	29,335	****	****	****	****	3.84	****	-0.55		0.80 (0.29, 2.33)	0.762
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05							
SV (183-day prior, 14-day gap)	31,491	****	****	****	****	2.79	****	-1.68	****	0.64 (0.24, 1.70)	0.367
ARBs (183-day prior, 14-day gap)	36,608	****	****	****	****	4.47	****	-1.00		0.04 (0.24, 1.70)	0.307

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

			Average	Average		Incidence Rate per	Risk per	Incidence Rate	Difference		
		Person	Average Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	•	Interval) ²	P-Value ²
Wedical Floudct	ivew osers	at Nisk	αι Νίοκ		61 - 90 Day		03613	reison rears	New Osers	iiitei vaij	r-value
Site-Adjusted Analysis					<u> </u>	<u> </u>					
SV (183-day prior, 14-day gap)	21,538	****	****	****	****	3.11	****				
ARBs (183-day prior, 14-day gap)	199,393	****	****	****	****	2.97	****	0.15	****	1.07 (0.43, 2.70)	0.882
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	15,962	****	****	****	****	2.67	****	2.67	****		
ARBs (183-day prior, 14-day gap)	15,962	****	****	****	****	0	****	2.67	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	21,507	****	****	****	****	3.12	****	3.12	****		
ARBs (183-day prior, 14-day gap)	28,996	****	****	****	****	0	****	5.12		-	
				9	91 - 180 Day	/s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	17,483	****	****	****	****	1.82	****	0.07	****	1.05 (0.45, 2.43)	0.911
ARBs (183-day prior, 14-day gap)	177,131	****	****	****	****	1.75	****	0.07		1.03 (0.43, 2.43)	0.511
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	11,400	****	****	****	****	2.46	****	0.61	****	1.33 (0.30, 5.96)	0.706
ARBs (183-day prior, 14-day gap)	11,400	****	****	****	****	1.84	****	0.01		1.33 (0.30, 3.30)	0.700
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	17,460	****	****	****	****	1.83	****	-0.33	****	0.84 (0.30, 2.31)	0.733
ARBs (183-day prior, 14-day gap)	25,575	****	****	****	****	2.16	****	-0.55		0.84 (0.30, 2.31)	0.733
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	10,720	****	****	****	****	0.92	****	-0.95	****	0.51 (0.12, 2.09)	0.346
ARBs (183-day prior, 14-day gap)	109,576	****	****	****	****	1.87	****	0.55		0.31 (0.12, 2.03)	0.540

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Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time

					Incidence		Incidence			
		Average	Average		Rate per	Risk per	Rate	Difference		
	Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
4,259	****	****	****	****	2.79	****	1 20	****	2.00 / 0.19, 22.06\	0.571
4,259	****	****	****	****	1.39	****	1.59		2.00 (0.18, 22.06)	0.571
Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
10,705	****	****	****	****	0.92	****	0.71	****	0.57/0.11 2.02)	0.499
15,297	****	****	****	****	1.63	****	-0.71		0.37 (0.11, 2.93)	0.433
			2	71 - 365 Da	ys					
7,356	****	****	****	****	0.62	****	-0.60	****	0.48 (0.07 2.58)	0.477
78,843	****	****	****	****	1.31	****	-0.09		0.48 (0.07, 3.38)	0.477
Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
2,066	****	****	****	****	2.58	****	2 50	****		
2,066	****	****	****	****	0	****	2.56		-	-
Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5		_				
7,349	****	****	****	****	0.62	****	1 11	****	0.27 / 0.04 (2.22)	0.375
10,577	****	****	****	****	1.73	****	-1.11		0.37 (0.04, 3.32)	0.373
	New Users Matched Cond 4,259 4,259 Matched Unco 10,705 15,297 7,356 78,843 Matched Cond 2,066 2,066 Matched Unco 7,349	Number of New Users at Risk Matched Conditional Ana 4,259 ***** Matched Unconditional A 10,705 ***** 15,297 ***** 7,356 ***** 78,843 ***** Matched Conditional Ana 2,066 ***** Matched Unconditional Ana 2,066 ***** Matched Unconditional A 7,349 *****	Person Person Person Number of Years Days New Users at Risk at Risk Matched Conditional Analysis; Calipo 4,259 **** ***** Matched Unconditional Analysis; Ca 10,705 **** ***** *****	Person Person Person Person Number of Years Days Years New Users at Risk A	Person Person Person Person Number of Years Days Years Number New Users at Risk at Risk at Risk at Risk of Events	Average	Number of Years Days Years Number Person New	Number of Person Number Person New Person New Person New Person New Person Person New Person New Person Person Person New Person Person Person Person New Person Person Person Person New Person Person Person Person Person Person Person New Person P	Number of Person Number Person New Person New Person Person Person New Person Person Person Person New Person Person Person New Person Person New Person Person New Person New	Number of Person Number of Number of Years Days Years Number Person New Person New Person Person Person Person New Person New Person Person

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 22. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

		Person	Average Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at	Number	per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Unknown											
Site-Adjusted Analysis											
SV (14-day gap, history of	8,082	****	****	****	****	1.84	****				
ARBs (-183, -1))								-0.67	****	0.71 (0.28, 1.78)	0.468
ARBs (14-day gap)	47,793	****	****	****	****	2.52	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	8,026	****	****	****	****	1.92	****				
ARBs (-183, -1))								0.64	****	1.50 (0.25, 8.98)	0.657
ARBs (14-day gap)	8,026	****	****	****	****	1.28	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	8,026	****	****	****	****	1.85	****				
ARBs (-183, -1))								-0.21	****	0.87 (0.27, 2.74)	0.807
ARBs (14-day gap)	8,026	****	****	****	****	2.07	****				
Race: American Indian											
Site-Adjusted Analysis											
SV (14-day gap, history of	133	****	****	****	****	0	****				
ARBs (-183, -1))								-1.36	****	-	-
ARBs (14-day gap)	1,948	****	****	****	****	1.36	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	131	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	131	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	131	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	131	****	****	****	****	0	****				

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Table 22. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

		Person	Average Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years at	Days at		Number	per 1,000 Person	•	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	Interval) ²	P-Value ²
Race: Asian											
Site-Adjusted Analysis											
SV (14-day gap, history of	1,070	****	****	****	****	0	****				
ARBs (-183, -1))								-0.81	****	-	-
ARBs (14-day gap)	7,811	****	****	****	****	0.81	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	1,026	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	1,026	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Uncondit	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	1,026	****	****	****	****	0	****				
ARBs (-183, -1))								-2.15	****	-	-
ARBs (14-day gap)	1,026	****	****	****	****	2.15	****				
Race: Black											
Site-Adjusted Analysis											
SV (14-day gap, history of	6,989	****	****	****	****	4.36	****				
ARBs (-183, -1))								-2.45	****	0.60 (0.31, 1.18)	0.139
ARBs (14-day gap)	55,801	****	****	****	****	6.8	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	6,967	****	****	****	****	4.11	****				
ARBs (-183, -1))								-4.11	****	0.50 (0.17, 1.46)	0.206
ARBs (14-day gap)	6,967	****	****	****	****	8.21	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Uncondit	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	6,967	****	****	****	****	4.36	****				
ARBs (-183, -1))								-1.17	****	0.74 (0.32, 1.70)	0.482
ARBs (14-day gap)	6,967	****	****	****	****	5.53	****				

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Table 22. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Person Years at		Incidence Rate per 1,000 Person		Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Pacific Islander											
Site-Adjusted Analysis		****	****	****	****	^	****				
SV (14-day gap, history of	61	4.4.4.4.4.	4.4.4.4.4.	4.4.4.4.	4 4 4 4 4	0	44444	9.07	****		
ARBs (-183, -1))	470	****	****	****	****	0.07	****	-8.97		-	-
ARBs (14-day gap)	478					8.97	****				
Fixed Ratio 1:1 Propensity So											
SV (14-day gap, history of	50	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	50	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	50	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	50	****	****	****	****	0	****				
Race: White											
Site-Adjusted Analysis											
SV (14-day gap, history of	32,805	****	****	****	****	2.48	****				
ARBs (-183, -1))								0.07	****	0.97 (0.66, 1.42)	0.858
ARBs (14-day gap)	223,252	****	****	****	****	2.4	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	32,796	****	****	****	****	3.61	****				,
ARBs (-183, -1))								0	****	1.00 (0.58, 1.72)	1
ARBs (14-day gap)	32,796	****	****	****	****	3.61	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	32,796	****	****	****	****	2.48	****				
ARBs (-183, -1))								-0.16	****	0.89 (0.55, 1.44)	0.647
ARBs (14-day gap)	32,796	****	****	****	****	2.63	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

						Incidence		Incidence			
			Average	•		Rate per	Risk per	Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Race: Unknown											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	8,082	****	****	****	****	1.84	****	-0.67	****	0.71 (0.28, 1.78)	0.468
ARBs (183-day prior, 14-day gap)	47,793	****	****	****	****	2.52	****	-0.07		0.71 (0.28, 1.78)	0.408
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	8,026	****	****	****	****	1.92	****	0.64	****	1.50 (0.25, 8.98)	0.657
ARBs (183-day prior, 14-day gap)	8,026	****	****	****	****	1.28	****	0.04		1.30 (0.23, 6.96)	0.657
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	8,026	****	****	****	****	1.85	****	-0.21	****	0.87 (0.27, 2.74)	0.807
ARBs (183-day prior, 14-day gap)	8,026	****	****	****	****	2.07	****	-0.21		0.87 (0.27, 2.74)	0.807
					0 - 30 Days	3					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	8,082	****	****	****	****	5.14	****	1 72	****	1 42 (0 41	0.570
ARBs (183-day prior, 14-day gap)	47,793	****	****	****	****	3.41	****	1.73		1.43 (0.41, 5.01)	0.579
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	8,026	****	****	****	****	5.35	****	г эг	****		
ARBs (183-day prior, 14-day gap)	8,026	****	****	****	****	0	****	5.35		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	8,026	****	****	****	****	5.17	****	Г 17	****		
ARBs (183-day prior, 14-day gap)	8,026	****	****	****	****	0	****	5.17	ran ran ran ran	-	-
					31 - 60 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	6,161	****	****	****	****	0	****	-2.52	****		
ARBs (183-day prior, 14-day gap)	44,551	****	****	****	****	2.52	****	-2.32		-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹						-	
SV (183-day prior, 14-day gap)	5,627	****	****	****	****	0	****	2.00	****		
ARBs (183-day prior, 14-day gap)	5,627	****	****	****	****	2.93	****	-2.93	****	-	-
Fixed Ratio 1:1 Propensity Score	· · · · · · · · · · · · · · · · · · ·	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	6,121	****	****	****	****	0	****	F 66	****		
ARBs (183-day prior, 14-day gap)	7,377	****	****	****	****	5.66	****	-5.66	4.4.4.4.4.	-	-
7	·				61 - 90 Day	s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	4,181	****	****	****	****	3.22	****	1.65	****	2 10 / 0 24 10 50\	0.488
ARBs (183-day prior, 14-day gap)	33,264	****	****	****	****	1.57	****	1.05		2.18 (0.24, 19.59)	0.466
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,880	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	2,880	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	4,154	****	****	****	****	3.24	****	3.24	****		
ARBs (183-day prior, 14-day gap)	5,599	****	****	****	****	0	****	5.24		-	
				9	1 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	3,352	****	****	****	****	1.54	****	-1.75	****	0.46 (0.06, 3.47)	0.453
ARBs (183-day prior, 14-day gap)	28,534	****	****	****	****	3.29	****	-1.75		0.40 (0.00, 3.47)	0.433
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,957	****	****	****	****	0	****	2.50	****		
ARBs (183-day prior, 14-day gap)	1,957	****	****	****	****	3.59	****	-3.59		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	3,332	****	****	****	****	1.55	****	-1.98	****	0.43 (0.05, 4.18)	0.47
ARBs (183-day prior, 14-day gap)	4,741	****	****	****	****	3.52	****	-1.98		0.45 (0.05, 4.18)	0.47

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Mark Control Day door	Number of	Person Years	Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk		of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Cita Adiustad Applusia				1	81 - 270 Da	ys					
Site-Adjusted Analysis	2.124	****	****	****	****	0	****				
SV (183-day prior, 14-day gap)	2,124	****	****	****	****	•	****	-2.06	****	-	-
ARBs (183-day prior, 14-day gap)	16,765				7- 1- 1- 1- 1-	2.06	4. 4. 4. 4.				
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	719	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	719	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco			•							
SV (183-day prior, 14-day gap)	2,117	****	****	****	****	0	****	-1.85	****	_	_
ARBs (183-day prior, 14-day gap)	2,716	****	****	****	****	1.85	****	1.05			
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,453	****	****	****	****	0	****	-1.16	****	_	_
ARBs (183-day prior, 14-day gap)	11,720	****	****	****	****	1.16	****	-1.10		_	
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	333	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	333	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	1,449	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	1,839	****	****	****	****	0	****	0		-	-
Race: American Indian	·										
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	133	****	****	****	****	0	****	1.20	****		
ARBs (183-day prior, 14-day gap)	1,948	****	****	****	****	1.36	****	-1.36	4. 4. 4. 4. 4.	-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	131	****	****	****	****	0	****		****		
ARBs (183-day prior, 14-day gap)	131	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	131	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	131	****	****	****	****	0	****	U		-	
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	133	****	****	****	****	0	****	-6.38	****	_	_
ARBs (183-day prior, 14-day gap)	1,948	****	****	****	****	6.38	****	-0.38		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	131	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	131	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	131	****	****	****	****	0	****	0	****	_	
ARBs (183-day prior, 14-day gap)	131	****	****	****	****	0	****	0			
					31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	101	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	1,839	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	97	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	97	****	****	****	****	0	****	<u> </u>		<u> </u>	
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	101	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	122	****	****	****	****	0	****	O			

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

			Avenere	Average		Incidence	Dieleman	Incidence Rate	Difference		
		Person	Average Person	Average Person		Rate per 1,000	Risk per 1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years		Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Madical Duadous			Days				_	• '	• •	Interval) ²	P-Value ²
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Osers	intervaij	P-value
Site-Adjusted Analysis					61 - 90 Day	S					
	62	****	****	****	****	0	****				
SV (183-day prior, 14-day gap)	1,233	****	****	****	****	0	****	0	****	-	-
ARBs (183-day prior, 14-day gap)	•					U					
Fixed Ratio 1:1 Propensity Score		****	ilysis; Calip	er= 0.05 ****	****		****				
SV (183-day prior, 14-day gap)	49	****	****	****	****	0	****	0	****	-	_
ARBs (183-day prior, 14-day gap)	49					0	****				
Fixed Ratio 1:1 Propensity Score		nditional A	nalysis; Ca	!iper= 0.0!	****		****				
SV (183-day prior, 14-day gap)	63					0		0	****	-	_
ARBs (183-day prior, 14-day gap)	91	****	****	****	****	0	****				
				9	180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	55	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	1,023	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	41	****	****	****	****	0	****	0	****	_	
ARBs (183-day prior, 14-day gap)	41	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	55	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	85	****	****	****	****	0	****	U		-	
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	32	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	550	****	****	****	****	0	****	U		-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score SV (183-day prior, 14-day gap)	Number of New Users Matched Cond	Person Years at Risk litional Ana *****	Person Days at Risk	Average Person Years at Risk er= 0.05 ¹ *****	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
ARBs (183-day prior, 14-day gap)	15	****	****	****	****	0	****	0	4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	33	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	44	****	****	****	****	0	****	0			
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	19	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	369	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****		_
ARBs (183-day prior, 14-day gap)	****	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	23	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	27	****	****	****	****	0	****				
Race: Asian											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,070	****	****	****	****	0	****	-0.81	****	_	_
ARBs (183-day prior, 14-day gap)	7,811	****	****	****	****	0.81	****	0.01			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,026	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	1,026	****	****	****	****	0	****	U		-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

						Incidence		Incidence			
			Average	Average		Rate per	Risk per	Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk		of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.05							
SV (183-day prior, 14-day gap)	1,026	****	****	****	****	0	****	-2.15	****	_	_
ARBs (183-day prior, 14-day gap)	1,026	****	****	****	****	2.15	****	-2.15		_	
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,070	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	7,811	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,026	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	1,026	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	1,026	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	1,026	****	****	****	****	0	****	0			
					31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	775	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	7,366	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond		lysis; Calip								
SV (183-day prior, 14-day gap)	698	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	698	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco			•							
SV (183-day prior, 14-day gap)	743	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	957	****	****	****	****	0	****	J			

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

		_	Average	_		Incidence Rate per	Risk per	Incidence Rate	Difference	Hazard Ratio	
		Person	Person	Person		1,000	1,000	Difference	in Risk	(95% Confidence	Wald
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	•	
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	515	****	****	****	****	0	****	-2.16	****	_	_
ARBs (183-day prior, 14-day gap)	5,969	****	****	****	****	2.16	****	2.10			
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	385	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	385	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	499	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	769	****	****	****	****	0	****	0		-	-
				9	1 - 180 Day	/s					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	410	****	****	****	****	0	****	-1.04	****		
ARBs (183-day prior, 14-day gap)	5,294	****	****	****	****	1.04	****	-1.04		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	264	****	****	****	****	0	****		****		
ARBs (183-day prior, 14-day gap)	264	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	397	****	****	****	****	0	****	0.22	****		
ARBs (183-day prior, 14-day gap)	678	****	****	****	****	8.23	****	-8.23	4. 4. 4. 4. 4.	-	-
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	269	****	****	****	****	0	****	1 55	****		
ARBs (183-day prior, 14-day gap)	3,215	****	****	****	****	1.55	****	-1.55	and the the the	-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score	Number of New Users Matched Cond	Person Years at Risk litional Ana	Average Person Days at Risk llysis; Calip	Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	100	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	100	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	262	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	401	****	****	****	****	0	****	-			
				2	71 - 365 Da	ys					
Site-Adjusted Analysis		****	****	****	****		****				
SV (183-day prior, 14-day gap)	184					0		0	****	_	-
ARBs (183-day prior, 14-day gap)	2,248	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond										
SV (183-day prior, 14-day gap)	55	****	****	****	****	0	****	0	****	_	
ARBs (183-day prior, 14-day gap)	55	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	179	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	261	****	****	****	****	0	****			<u>-</u>	
Race: Black											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	6,989	****	****	****	****	4.36	****	-2.45	****	0.60 (0.31, 1.18)	0.139
ARBs (183-day prior, 14-day gap)	55,801	****	****	****	****	6.8	****	2.43		0.00 (0.51, 1.10)	U.133
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	6,967	****	****	****	****	4.11	****	4 11	****	0.50/0.17 1.46\	0.206
ARBs (183-day prior, 14-day gap)	6,967	****	****	****	****	8.21	****	-4.11	and the state of	0.50 (0.17, 1.46)	0.206

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

						Incidence		Incidence			
			Average	Average		Rate per	Risk per	Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05							
SV (183-day prior, 14-day gap)	6,967	****	****	****	****	4.36	****	-1.17	****	0.74 (0.32, 1.70)	0.482
ARBs (183-day prior, 14-day gap)	6,967	****	****	****	****	5.53	****	-1.17		0.74 (0.32, 1.70)	0.482
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	6,989	****	****	****	****	3.9	****	-9.75	****	0.28 (0.07, 1.14)	0.075
ARBs (183-day prior, 14-day gap)	55,801	****	****	****	****	13.65	****	-9.75		0.28 (0.07, 1.14)	0.075
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	6,967	****	****	****	****	4.04	****	-8.08	****	0.33 (0.07, 1.65)	0.178
ARBs (183-day prior, 14-day gap)	6,967	****	****	****	****	12.12	****	-6.06		0.33 (0.07, 1.03)	0.178
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	6,967	****	****	****	****	3.91	****	-10.53	****	0.27 (0.06, 1.26)	0.095
ARBs (183-day prior, 14-day gap)	6,967	****	****	****	****	14.44	****	-10.55		0.27 (0.00, 1.20)	0.093
				\$	31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	5,495	****	****	****	****	5.59	****	-1.82	****	0.76 (0.18, 3.21)	0.711
ARBs (183-day prior, 14-day gap)	52,264	****	****	****	****	7.4	****	-1.02		0.70 (0.18, 3.21)	0.711
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	5,052	****	****	****	****	6.92	****	0	****	1.00 (0.14, 7.10)	1
ARBs (183-day prior, 14-day gap)	5,052	****	****	****	****	6.92	****	0		1.00 (0.14, 7.10)	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	5,480	****	****	****	****	5.6	****	1.19	****	1.29 (0.18, 9.14)	0.801
ARBs (183-day prior, 14-day gap)	6,431	****	****	****	****	4.41	****	1.19		1.23 (0.10, 3.14)	0.001

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Wicarda Froduct	New Osers	at Mak	at Mak		61 - 90 Day		03013	T CISON TCUIS	IVEW OSCIS	intervary	- Value
Site-Adjusted Analysis						-					
SV (183-day prior, 14-day gap)	3,368	****	****	****	****	8.15	****	4.52	****	4.25 / 0.20 5.27	0.764
ARBs (183-day prior, 14-day gap)	37,443	****	****	****	****	6.61	****	1.53	****	1.25 (0.29, 5.37)	0.764
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	alysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	2,215	****	****	****	****	6.58	****	6.50	****		
ARBs (183-day prior, 14-day gap)	2,215	****	****	****	****	0	****	6.58	4.4.4.4.4.	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	Analysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	3,361	****	****	****	****	8.16	****	8.16	****		
ARBs (183-day prior, 14-day gap)	4,686	****	****	****	****	0	****	6.10			
				9	91 - 180 Day	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	2,573	****	****	****	****	2.18	****	-2.05	****	0.53 (0.07, 3.92)	0.533
ARBs (183-day prior, 14-day gap)	32,130	****	****	****	****	4.23	****			0.55 (0.07, 0.52)	
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	alysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,452	****	****	****	****	0	****	-5.49	****	_	_
ARBs (183-day prior, 14-day gap)	1,452	****	****	****	****	5.49	****	-5.45			
Fixed Ratio 1:1 Propensity Score	Matched Unco		Analysis; Ca	liper= 0.0							
SV (183-day prior, 14-day gap)	2,568	****	****	****	****	2.18	****	-2.3	****	0.49 (0.05, 4.74)	0.54
ARBs (183-day prior, 14-day gap)	3,985	****	****	****	****	4.48	****	-2.3		0.49 (0.03, 4.74)	0.54
				1	81 - 270 Da	iys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	1,423	****	****	****	****	3.49	****	-0.69	****	0.85 (0.11, 6.44)	0.872
ARBs (183-day prior, 14-day gap)	17,230	****	****	****	****	4.18	****	0.05		0.00 (0.11, 0.44)	0.072

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product Fixed Ratio 1:1 Propensity Score	Number of New Users Matched Cond	Person Years at Risk itional Ana	Person Days at Risk	Average Person Years at Risk er= 0.051	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
SV (183-day prior, 14-day gap)	415	****	****	****	****	0	****		****		
ARBs (183-day prior, 14-day gap)	415	****	****	****	****	14.54	****	-14.54	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	1,420	****	****	****	****	3.49	****	1	****	1 42 / 0 00 22 72\	0.004
ARBs (183-day prior, 14-day gap)	2,097	****	****	****	****	2.49	****	1		1.42 (0.09, 22.73)	0.804
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	965	****	****	****	****	4.89	****	1.99	****	1.80 (0.22, 14.65)	0.585
ARBs (183-day prior, 14-day gap)	11,238	****	****	****	****	2.9	****	1.99		1.80 (0.22, 14.03)	0.363
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	194	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	194	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	966	****	****	****	****	4.89	****	1.24	****	1 22 / 0 00 21 02	0.046
ARBs (183-day prior, 14-day gap)	1,324	****	****	****	****	3.64	****	1.24		1.32 (0.08, 21.03)	0.846
Race: Pacific Islander											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	61	****	****	****	****	0	****	-8.97	****	_	_
ARBs (183-day prior, 14-day gap)	478	****	****	****	****	8.97	****	-0.37		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	50	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	50	****	****	****	****	0	****	U		-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

			Ā			Incidence	D: 1	Incidence	D:((
		_	U	Average		Rate per	Risk per	Rate	Difference	Hazard Ratio	
		Person	Person	Person	_	1,000	1,000	Difference	in Risk		147-1-I
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk		of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.05							
SV (183-day prior, 14-day gap)	50	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	50	****	****	****	****	0	****	U		_	_
					0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	61	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	478	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	50	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	50	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	50	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	50	****	****	****	****	0	****	0		-	-
				;	31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	52	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	447	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	41	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	41	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (183-day prior, 14-day gap)	45	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	46	****	****	****	****	0	****	U		-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

						Incidence		Incidence			
			Average	Average		Rate per	Risk per	Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	34	****	****	****	****	0	****	-34.82	****		
ARBs (183-day prior, 14-day gap)	362	****	****	****	****	34.82	****	-54.62		-	
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	21	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	21	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	29	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	39	****	****	****	****	0	****	0		_	
				9	91 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	22	****	****	****	****	0	****	-17.55	****	_	_
ARBs (183-day prior, 14-day gap)	337	****	****	****	****	17.55	****	-17.55			
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	12	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	12	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0	5				_		
SV (183-day prior, 14-day gap)	19	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	35	****	****	****	****	0	****	U		-	-

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

	Number of	Person Years	Average Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	• •	Interval) ²	P-Value ²
					81 - 270 Da	ys				,	
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	13	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	192	****	****	****	****	0	****	0		<u>-</u>	
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	11	****	****	****	****	0	****	0	****		
ARBs (183-day prior, 14-day gap)	21	****	****	****	****	0	****	<u> </u>			
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	138	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score		ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	****	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score				•							
SV (183-day prior, 14-day gap)	****	****	****	****	****	0	****	0	****	_	_
ARBs (183-day prior, 14-day gap)	15	****	****	****	****	0	****				
Race: White											
					Overall						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	32,805	****	****	****	****	2.48	****	0.07	****	0.97 (0.66, 1.42)	0.858
ARBs (183-day prior, 14-day gap)	223,252	****	****	****	****	2.4	****	0.07			0.000

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score											
SV (183-day prior, 14-day gap)	32,796	****	*****	****	****	3.61	****				
ARBs (183-day prior, 14-day gap)	32,796	****	****	****	****	3.61	****	0	****	1.00 (0.58, 1.72)	1
Fixed Ratio 1:1 Propensity Score		onditional A	nalvsis: Ca	liper= 0.0!	5	3.01					
SV (183-day prior, 14-day gap)	32,796	****	****	****	****	2.48	****				
ARBs (183-day prior, 14-day gap)	32,796	****	****	****	****	2.63	****	-0.16	****	0.89 (0.55, 1.44)	0.647
Titles (100 day prior) 11 day gap)	32,730				0 - 30 Days						
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	32,805	****	****	****	****	3.69	****		****	0.75 / 0.00 / 40)	
ARBs (183-day prior, 14-day gap)	223,252	****	****	****	****	4.81	****	-1.11	****	0.75 (0.38, 1.49)	0.413
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	32,796	****	****	****	****	3.37	****	2.11	****	0.62 / 0.26 1.40	0.20
ARBs (183-day prior, 14-day gap)	32,796	****	****	****	****	5.48	****	-2.11		0.62 (0.26, 1.48)	0.28
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	32,796	****	****	****	****	3.69	****	2.02	****	0.64 (0.39 1.46)	0.207
ARBs (183-day prior, 14-day gap)	32,796	****	****	****	****	5.73	****	-2.03		0.64 (0.28, 1.46)	0.287
					31 - 60 Day	S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	26,529	****	****	****	****	3.29	****	0.49	****	1.16 (0.50, 2.74)	0.727
ARBs (183-day prior, 14-day gap)	209,760	****	****	****	****	2.81	****	0.45		1.10 (0.30, 2.74)	0.727
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	24,768	****	****	****	****	3.9	****	0	****	1.00 (0.32, 3.10)	1
ARBs (183-day prior, 14-day gap)	24,768	****	****	****	****	3.9	****	<u> </u>		1.00 (0.32, 3.10)	1
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	26,520	****	****	****	****	3.3	****	-1.17	****	0.74 (0.27, 2.04)	0.564
ARBs (183-day prior, 14-day gap)	30,621	****	****	****	****	4.47	****	-1.1/		0.74 (0.27, 2.04)	0.304

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

	Number of	Person Years	Person Days	Average Person Years	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
C' Al' I LA L '					61 - 90 Day	S					
Site-Adjusted Analysis		district dist	4.4.4.4.	at at at at at	4.4.4.4.						
SV (183-day prior, 14-day gap)	18,317	****	****	****	****	2.92	****	0.74	****	1.35 (0.47, 3.85)	0.575
ARBs (183-day prior, 14-day gap)	165,181	****	****	****	****	2.18	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	13,479	****	****	****	****	3.15	****	3.15	****		
ARBs (183-day prior, 14-day gap)	13,479	****	****	****	****	0	****	5.15		-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	Analysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	18,311	****	****	****	****	2.92	****	2.02	****		
ARBs (183-day prior, 14-day gap)	24,143	****	****	****	****	0	****	2.92		-	-
				9	91 - 180 Day	/S					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	14,962	****	****	****	****	2.48	****	0.70	****	1 47 (0 66 2 25)	0.246
ARBs (183-day prior, 14-day gap)	146,922	****	****	****	****	1.69	****	0.79		1.47 (0.66, 3.25)	0.346
Fixed Ratio 1:1 Propensity Score	Matched Cond	ditional Ana	lvsis: Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	9,689	****	****	****	****	4.33	****	0.70	****	1 22 / 2 27 2 22)	
ARBs (183-day prior, 14-day gap)	9,689	****	****	****	****	3.61	****	0.72	****	1.20 (0.37, 3.93)	0.763
Fixed Ratio 1:1 Propensity Score	Matched Unco	onditional A	Analysis; Ca	liper= 0.0	5						
SV (183-day prior, 14-day gap)	14,956	****	****	****	****	2.48	****	0.42	****	4.20 (0.44 2.24)	0.724
ARBs (183-day prior, 14-day gap)	21,311	****	****	****	****	2.06	****	0.42	****	1.20 (0.44, 3.31)	0.724
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	9,241	****	****	****	****	1.07	****	0.67	****	0.63/0.45 3.64\	0.530
ARBs (183-day prior, 14-day gap)	92,122	****	****	****	****	1.74	****	-0.67	nen nen nen nen nen	0.63 (0.15, 2.64)	0.529

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Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time

Medical Product	Number of New Users	Person Years at Risk	Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score I	Matched Cond										
SV (183-day prior, 14-day gap)	3,652	****	****	****	****	3.25	****	0	****	1.00 (0.14, 7.10)	1
ARBs (183-day prior, 14-day gap)	3,652	****	****	****	****	3.25	****	0		1.00 (0.14, 7.10)	
Fixed Ratio 1:1 Propensity Score I	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	9,237	****	****	****	****	1.07	****	-0.08	****	0.96 (0.16, 5.74)	0.963
ARBs (183-day prior, 14-day gap)	12,898	****	****	****	****	1.15	****	-0.08		0.90 (0.10, 3.74)	0.903
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (183-day prior, 14-day gap)	6,366	****	****	****	****	0.72	****	-0.75	****	0.40 / 0.07 (2.65)	0.487
ARBs (183-day prior, 14-day gap)	66,936	****	****	****	****	1.47	****	-0.75		0.49 (0.07, 3.65)	0.467
Fixed Ratio 1:1 Propensity Score I	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (183-day prior, 14-day gap)	1,767	****	****	****	****	3.02	****	2.02	****		
ARBs (183-day prior, 14-day gap)	1,767	****	****	****	****	0	****	3.02	4.4.4.4.4.	-	-
Fixed Ratio 1:1 Propensity Score I	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (183-day prior, 14-day gap)	6,363	****	****	****	****	0.72	****	1 21	****	0.37/0.04 3.37\	0.200
ARBs (183-day prior, 14-day gap)	8,999	****	****	****	****	2.03	****	-1.31		0.37 (0.04, 3.27)	0.368

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 24. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person S Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Site-Adjusted Analysis											
SV (14-day gap, history of	49,629	****	****	****	****	2.43	****				
ACEI (-14, -1))								-4.3	****	0.34 (0.25, 0.47)	<0.001
ACEI (14-day gap)	695,068	****	****	****	****	6.74	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	0.05						
SV (14-day gap, history of	49,628	****	****	****	****	2.52	****				_
ACEI (-14, -1))								-6.73	****	0.27 (0.17, 0.43)	< 0.001
ACEI (14-day gap)	49,628	****	****	****	****	9.26	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	onal Analy	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	49,628	****	****	****	****	2.43	****	_		_	
ACEI (-14, -1))								-3.65	****	0.37 (0.26, 0.53)	< 0.001
ACEI (14-day gap)	49,628	****	****	****	****	6.08	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 25. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-Up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Cita Adinated Applicate					Overall						
Site-Adjusted Analysis	40.620	****	****	****	****	2.42	****				
SV (14-day prior, 14-day gap)	49,629	****	****	****	****	2.43	****	-4.3	****	0.34 (0.25, 0.47)	< 0.001
ACEI (14-day prior, 14-day gap)	695,068				4444	6.74	44444				
Fixed Ratio 1:1 Propensity Score											
SV (14-day prior, 14-day gap)	49,628	****	****	****	****	2.52	****	-6.73	****	0.27 (0.17, 0.43)	<0.001
ACEI (14-day prior, 14-day gap)	49,628	****	****	****	****	9.26	****	0.75		0.27 (0.27) 0.10)	
Fixed Ratio 1:1 Propensity Score	Matched Unco			•							
SV (14-day prior, 14-day gap)	49,628	****	****	****	****	2.43	****	-3.65	****	0.37 (0.26, 0.53)	<0.001
ACEI (14-day prior, 14-day gap)	49,628	****	****	****	****	6.08	****	-3.05		0.37 (0.20, 0.33)	\0.001
					0 - 30 Days						
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	49,629	****	****	****	****	3.93	****	-11.42	****	0.25 (0.15, 0.42)	<0.001
ACEI (14-day prior, 14-day gap)	695,068	****	****	****	****	15.35	****	-11.42		0.23 (0.13, 0.42)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (14-day prior, 14-day gap)	49,628	****	****	****	****	3.77	****	12.06	****	0.33 / 0.43 . 0.44	10,001
ACEI (14-day prior, 14-day gap)	49,628	****	****	****	****	16.83	****	-13.06	4. 4. 4. 4.	0.22 (0.12, 0.41)	<0.001
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0	5						
SV (14-day prior, 14-day gap)	49,628	****	****	****	****	3.93	****	44.24	****	0.35 / 0.44 . 0.45\	.0.001
ACEI (14-day prior, 14-day gap)	49,628	****	****	****	****	15.26	****	-11.34	****	0.25 (0.14, 0.45)	<0.001
71 7 7 7 7 7 7	,				31 - 60 Day	S					
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	37,404	****	****	****	****	3.94	****	2.4	****	0.65 / 0.35 / 4.33\	0.400
ACEI (14-day prior, 14-day gap)	638,536	****	****	****	****	6.05	****	-2.1	~ ~ ~ ~ ~	0.65 (0.35, 1.23)	0.188

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Table 25. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-Up Time

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Fixed Ratio 1:1 Propensity Score					0. 210	. cu.s	000.0	7 613611 1 6413	11011 05015	e.r va.r	7 4.40
SV (14-day prior, 14-day gap)	34,305	****	****	****	****	2.92	****	2.00	****	0.40 / 0.45 . 4.40	0.000
ACEI (14-day prior, 14-day gap)	34,305	****	****	****	****	6.8	****	-3.89	****	0.43 (0.16, 1.12)	0.082
Fixed Ratio 1:1 Propensity Score		nditional A	nalysis; Ca	liper= 0.0!	5						
SV (14-day prior, 14-day gap)	37,403	****	****	****	****	3.94	****	1.2	****	0.74 / 0.24 1.62	0.46
ACEI (14-day prior, 14-day gap)	45,509	****	****	****	****	5.25	****	-1.3		0.74 (0.34, 1.63)	0.46
					61 - 90 Day	S					
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	25,147	****	****	****	****	2.69	****	-3.09	****	0.47 (0.19, 1.13)	0.092
ACEI (14-day prior, 14-day gap)	463,084	****	****	****	****	5.78	****	-5.05		0.47 (0.13, 1.13)	0.032
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (14-day prior, 14-day gap)	17,306	****	****	****	****	1.67	****	-5	****	0.25 (0.05, 1.18)	0.08
ACEI (14-day prior, 14-day gap)	17,306	****	****	****	****	6.67	****	-5		0.23 (0.03, 1.18)	0.08
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.0!							
SV (14-day prior, 14-day gap)	25,146	****	****	****	****	2.69	****	-4.2	****	0.39 (0.14, 1.04)	0.06
ACEI (14-day prior, 14-day gap)	34,002	****	****	****	****	6.89	****	-4.2		0.59 (0.14, 1.04)	0.00
				g	91 - 180 Day	/S					
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	19,929	****	****	****	****	0.78	****	-3.61	****	0.18 (0.06, 0.55)	0.003
ACEI (14-day prior, 14-day gap)	397,797	****	****	****	****	4.39	****				
Fixed Ratio 1:1 Propensity Score	Matched Cond										
SV (14-day prior, 14-day gap)	11,912	****	****	****	****	0.59	****	-2.34	****	0.20 (0.02, 1.71)	0.142
ACEI (14-day prior, 14-day gap)	11,912	****	****	****	****	2.93	****	2.54		0.20 (0.02, 1.71)	0.142
Fixed Ratio 1:1 Propensity Score				-							
SV (14-day prior, 14-day gap)	19,928	****	****	****	****	0.78	****	-1.11	****	0.40 (0.11, 1.45)	0.162
ACEI (14-day prior, 14-day gap)	29,452	****	****	****	****	1.89	****			0.10 (0.11) 1.10)	
				1	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	12,764	****	****	****	****	1.9	****	-2.22	****	0.46 (0.19, 1.12)	0.086
ACEI (14-day prior, 14-day gap)	235,571	****	****	****	****	4.12	****			()	

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Table 25. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-Up Time

		Person	Person	Average Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio	Mr.I.I
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (14-day prior, 14-day gap)	4,378	****	****	****	****	2.77	****	-1.39	****	0.67 (0.11, 3.99)	0.657
ACEI (14-day prior, 14-day gap)	4,378	****	****	****	****	4.16	****	-1.59		0.67 (0.11, 5.99)	0.057
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (14-day prior, 14-day gap)	12,766	****	****	****	****	1.9	****	-1.65	****	0.52 (0.18, 1.48)	0.222
ACEI (14-day prior, 14-day gap)	17,106	****	****	****	****	3.55	****	-1.05		0.52 (0.16, 1.46)	0.222
				2	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	9,031	****	****	****	****	1.5	****	-2.05	****	0.42 / 0.12 1.21)	0.133
ACEI (14-day prior, 14-day gap)	164,784	****	****	****	****	3.54	****	-2.05		0.42 (0.13, 1.31)	0.155
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹							
SV (14-day prior, 14-day gap)	2,024	****	****	****	****	0	****		****		
ACEI (14-day prior, 14-day gap)	2,024	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.0!	5						
SV (14-day prior, 14-day gap)	9,030	****	****	****	****	1.5	****	3.50	****	0.26 / 0.10 1.22	0.124
ACEI (14-day prior, 14-day gap)	11,426	****	****	****	****	4.09	****	-2.59	-1	0.36 (0.10, 1.32)	0.124

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 26. Effect Estimates forNew Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)

	Number of	Person Years at	Average Person Days at	Average Person	Numbor	Incidence Rate	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	Interval)	P-Value
No Angioedema (-183, -1)	New Osers	Nisk	Misk	Misk	OI EVEILES	rears	OJCIJ	icuis	New Osers	intervaly	Value
Site-Adjusted Analysis											
SV (14-day gap, history of	49,583	****	****	****	****	2.37	****				
ACEI (-14, -1))	,							-4.1	****	0.35 (0.25, 0.48)	< 0.001
ACEI (14-day gap)	694,204	****	****	****	****	6.48	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	49,582	****	****	****	****	2.42	****				
ACEI (-14, -1))								-6.42	****	0.27 (0.17, 0.43)	< 0.001
ACEI (14-day gap)	49,582	****	****	****	****	8.84	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	49,582	****	****	****	****	2.37	****				
ACEI (-14, -1))								-3.47	****	0.38 (0.27, 0.55)	< 0.001
ACEI (14-day gap)	49,582	****	****	****	****	5.85	****				
Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	46	****	****	****	****	77.34	****				
ACEI (-14, -1))								-190.86	****	0.26 (0.04, 1.91)	0.186
ACEI (14-day gap)	864	****	****	****	****	268.2	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	39	****	****	****	****	186.22	****				
ACEI (-14, -1))								-186.22	****	0.50 (0.05, 5.51)	0.571
ACEI (14-day gap)	39	****	****	****	****	372.44	****				
Fixed Ratio 1:1 Propensity So	core Matched										
SV (14-day gap, history of	39	****	****	****	****	88.73	****				
ACEI (-14, -1))								-143.29	****	0.37 (0.04, 3.58)	0.392
ACEI (14-day gap)	39	****	****	****	****	232.02	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 27: Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
No Angioedema (ever, -1)										·	
Site-Adjusted Analysis											
SV (14-day gap, history of	49,296	****	****	****	****	2.26	****				
ACEI (-14, -1))								-3.61	****	0.37 (0.26, 0.51)	< 0.001
ACEI (14-day gap)	687,748	****	****	****	****	5.88	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	49,295	****	****	****	****	2.54	****				
ACEI (-14, -1))								-4.87	****	0.34 (0.22, 0.55)	<0.001
ACEI (14-day gap)	49,295	****	****	****	****	7.41	****				
Fixed Ratio 1:1 Propensity S	core Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	49,295	****	****	****	****	2.26	****				
ACEI (-14, -1))								-2.7	****	0.43 (0.29, 0.62)	<0.001
ACEI (14-day gap)	49,295	****	****	****	****	4.97	****				
Angioedema (ever, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	333	****	****	****	****	31.78	****				
ACEI (-14, -1))								-65.3	****	0.30 (0.10, 0.93)	0.037
ACEI (14-day gap)	7,320	****	****	****	****	97.08	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	327	****	****	****	****	35.77	****				
ACEI (-14, -1))								-107.3	****	0.25 (0.05, 1.18)	0.08
ACEI (14-day gap)	327	****	****	****	****	143.06	****				
Fixed Ratio 1:1 Propensity S	core Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	327	****	****	****	****	32.31	****				
ACEI (-14, -1))								-88.41	****	0.23 (0.07, 0.80)	0.021
ACEI (14-day gap)	327	****	****	****	****	120.71	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 28. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
No Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	44,259	****	****	****	****	2.23	****				
ACEI (-14, -1))								-4.24	****	0.33 (0.23, 0.46)	< 0.001
ACEI (14-day gap)	584,072	****	****	****	****	6.47	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	44,253	****	****	****	****	2.21	****				
ACEI (-14, -1))								-5.94	****	0.27 (0.16, 0.45)	< 0.001
ACEI (14-day gap)	44,253	****	****	****	****	8.15	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	44,253	****	****	****	****	2.23	****				
ACEI (-14, -1))								-3	****	0.40 (0.27, 0.59)	<0.001
ACEI (14-day gap)	44,253	****	****	****	****	5.22	****				
Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	5,370	****	****	****	****	4.27	****				
ACEI (-14, -1))								-4.05	****	0.49 (0.23, 1.04)	0.063
ACEI (14-day gap)	110,996	****	****	****	****	8.31	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.051						
SV (14-day gap, history of	5,365	****	****	****	****	4.36	****				
ACEI (-14, -1))								-8.72	****	0.33 (0.11, 1.03)	0.057
ACEI (14-day gap)	5,365	****	****	****	****	13.09	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	5,365	****	****	****	****	4.27	****				
ACEI (-14, -1))								-4.11	****	0.47 (0.20, 1.14)	0.094
ACEI (14-day gap)	5,365	****	****	****	****	8.38	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



			Average		• •	Incidence	Risk per	Incidence Rate	Difference in		
		Person	Person	Person	Number	Rate per	1,000	Difference per	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Sex: Male											
					Overa	11					
Site-Adjusted Analysis											
SV (14-day gap, history of	34,743	****	****	****	****	2.57	****				
ACEI (-14, -1))								-3.41	****	0.41 (0.28, 0.58)	<0.001
ACEI (14-day gap)	353,146	****	****	****	****	5.98	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	34,715	****	****	****	****	2.82	****				
ACEI (-14, -1))								-4.46	****	0.39 (0.23, 0.66)	< 0.001
ACEI (14-day gap)	34,715	****	****	****	****	7.28	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Calip	er= 0.05							
SV (14-day gap, history of	34,715	****	****	****	****	2.57	****				
ACEI (-14, -1))								-1.87	****	0.54 (0.35, 0.84)	0.006
ACEI (14-day gap)	34,715	****	****	****	****	4.44	****				
					0 - 30 Da	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	34,743	****	****	****	****	3.19	****				
ACEI (-14, -1))								-11.41	****	0.21 (0.11, 0.43)	<0.001
ACEI (14-day gap)	353,146	****	****	****	****	14.6	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	34,715	****	****	****	****	3.31	****				
ACEI (-14, -1))								-9.92	****	0.25 (0.12, 0.54)	<0.001
ACEI (14-day gap)	34,715	****	****	****	****	13.23	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor			per= 0.05							
SV (14-day gap, history of	34,715	****	****	****	****	3.19	****				
ACEI (-14, -1))								-8.46	****	0.27 (0.12, 0.58)	<0.001
ACEI (14-day gap)	34,715	****	****	****	****	11.65	****				

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,	• •		Average	Average		Incidence	Risk per	Incidence Rate	Difference in		
		Person	Person	Person	Number	Rate per	1,000	Difference per	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					31 - 60 D	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	26,387	****	****	****	****	4.46	****				
ACEI (-14, -1))								-1.13	****	0.79 (0.39, 1.62)	0.52
ACEI (14-day gap)	325,667	****	****	****	****	5.59	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	/sis; Calipe	r= 0.05 ¹							
SV (14-day gap, history of	24,158	****	****	****	****	3.44	****				
ACEI (-14, -1))								-0.69	****	0.83 (0.25, 2.73)	0.763
ACEI (14-day gap)	24,158	****	****	****	****	4.13	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	26,368	****	****	****	****	4.46	****				
ACEI (-14, -1))								0.49	****	1.09 (0.42, 2.83)	0.857
ACEI (14-day gap)	31,762	****	****	****	****	3.97	****				
					61 - 90 D	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	17,862	****	****	****	****	3.79	****		ale ale ale ale ale		
ACEI (-14, -1))								-0.95	****	0.80 (0.33, 1.98)	0.636
ACEI (14-day gap)	236,803	****	****	****	****	4.74	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi										
SV (14-day gap, history of	12,310	****	****	****	****	2.34	****				
ACEI (-14, -1))								-3.52	****	0.40 (0.08, 2.06)	0.273
ACEI (14-day gap)	12,310	****	****	****	****	5.86	****				
Fixed Ratio 1:1 Propensity Score											
SV (14-day gap, history of	17,847	****	****	****	****	3.79	****				
ACEI (-14, -1))								-0.58	****	0.87 (0.28, 2.66)	0.806
ACEI (14-day gap)	23,871	****	****	****	****	4.37	****				

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,	• •		Average	Average		Incidence	Risk per	Incidence Rate	Difference in		
		Person	Person	Person	Number	Rate per	1,000	Difference per	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					91 - 180 [Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	14,181	****	****	****	****	0.36	****				
ACEI (-14, -1))								-3.14	****	0.10 (0.01, 0.74)	0.024
ACEI (14-day gap)	203,937	****	****	****	****	3.5	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	/sis; Calipe	r= 0.05 1							
SV (14-day gap, history of	8,440	****	****	****	****	0.82	****				
ACEI (-14, -1))								-1.64	****	0.33 (0.03, 3.20)	0.341
ACEI (14-day gap)	8,440	****	****	****	****	2.47	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	14,171	****	****	****	****	0.36	****				
ACEI (-14, -1))								-1.26	****	0.22 (0.03, 1.79)	0.155
ACEI (14-day gap)	20,616	****	****	****	****	1.62	****				
					181 - 270	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	9,105	****	****	****	****	2.67	****				
ACEI (-14, -1))								-0.74	****	0.78 (0.32, 1.92)	0.587
ACEI (14-day gap)	120,273	****	****	****	****	3.41	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	/sis; Calipe	r= 0.05 ¹							
SV (14-day gap, history of	3,136	****	****	****	****	5.81	****				
ACEI (-14, -1))								1.94	****	1.50 (0.25, 8.98)	0.657
ACEI (14-day gap)	3,136	****	****	****	****	3.87	****				
Fixed Ratio 1:1 Propensity Score											
SV (14-day gap, history of	9,101	****	****	****	****	2.67	****				
ACEI (-14, -1))								0.56	****	1.23 (0.36, 4.25)	0.744
ACEI (14-day gap)	12,007	****	****	****	****	2.11	****				

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			Average	Average		Incidence	Risk per	Incidence Rate	Difference in		
		Person	Person	Person	Number	Rate per	1,000	Difference per	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					271 - 365	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	6,443	****	****	****	****	2.1	****				
ACEI (-14, -1))								-0.81	****	0.70 (0.22, 2.25)	0.553
ACEI (14-day gap)	84,138	****	****	****	****	2.91	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Analy	ysis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	1,481	****	****	****	****	0	****				
ACEI (-14, -1))								-3.62	****	-	-
ACEI (14-day gap)	1,481	****	****	****	****	3.62	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Uncor	nditional An	alysis; Cali _l	per= 0.05							
SV (14-day gap, history of	6,440	****	****	****	****	2.1	****				
ACEI (-14, -1))								-0.82	****	0.69 (0.16, 2.88)	0.608
ACEI (14-day gap)	8,010	****	****	****	****	2.92	****				
Sex: Female											
					Overa	<u> </u>					
Site-Adjusted Analysis											
SV (14-day gap, history of	14,886	****	****	****	****	2.09	****				
ACEI (-14, -1))								-5.43	****	0.26 (0.14, 0.49)	<0.001
ACEI (14-day gap)	341,922	****	****	****	****	7.53	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Analy	ysis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	14,885	****	****	****	****	2.94	****				
ACEI (-14, -1))								-8.82	****	0.25 (0.12, 0.54)	< 0.001
ACEI (14-day gap)	14,885	****	****	****	****	11.76	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Unco	nditional An	alysis; Calip	per= 0.05							
SV (14-day gap, history of	14,885	****	****	****	****	2.09	****				
ACEI (-14, -1))								-6.87	****	0.22 (0.11, 0.43)	< 0.001
ACEI (14-day gap)	14,885	****	****	****	****	8.96	****				

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Average Average Incidence Risk per Incidence Rate Difference in **Hazard Ratio** Person Person Person Number Rate per 1.000 Difference per Risk per (95% Confidence Wald Number of Years Years of 1.000 New 1.000 1.000 Days **Medical Product** Interval)2 P-Value² **New Users** at Risk at Risk at Risk Events **Person Years Person Years New Users** Users 0 - 30 Days **Site-Adjusted Analysis** **** **** **** **** SV (14-day gap, history of 14,886 5.67 **** -10.46 0.34 (0.15, 0.77) 0.01 ACEI (-14, -1)) **** **** **** ACEI (14-day gap) 341.922 16.13 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** **** **** SV (14-day gap, history of 14.885 5.91 -15.75 0.27 (0.11, 0.67) 0.005 ACEI (-14, -1)) **** **** **** **** 14.885 ACEI (14-day gap) 21.65 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 **** **** SV (14-day gap, history of 14,885 5.67 -16.55 0.25 (0.10, 0.61) 0.002 ACEI (-14, -1)) **** **** **** **** **** 22.22 14.885 ACEI (14-day gap) 31 - 60 Days **Site-Adjusted Analysis** **** **** **** **** 2.7 **** SV (14-day gap, history of 11.017 **** -3.82 0.42 (0.10, 1.69) 0.223 ACEI (-14, -1)) **** **** **** **** ACEI (14-day gap) 312.869 6.52 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** SV (14-day gap, history of 9,881 3.41 -3.41 **** 0.50 (0.09, 2.73) 0.423 ACEI (-14, -1)) **** **** **** **** ACEI (14-day gap) 9,881 6.83 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 **** SV (14-day gap, history of 11.016 **** 2.7 -2.590.52 (0.10, 2.68) 0.434 ACEI (-14, -1)) **** ACEI (14-day gap) 13,364 5.29

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Average Average Incidence Risk per Incidence Rate Difference in **Hazard Ratio** Person Person Number Rate per 1.000 Difference per Risk per Person (95% Confidence Wald Number of Years Years of 1.000 New 1.000 1.000 Days **Medical Product** Interval)2 P-Value² **New Users** at Risk at Risk at Risk Events **Person Years Person Years New Users** Users 61 - 90 Days **Site-Adjusted Analysis** **** **** **** 0 **** SV (14-day gap, history of 7,285 **** -6.88ACEI (-14, -1)) **** **** **** ACEI (14-day gap) 226.281 6.88 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** **** **** 0 SV (14-day gap, history of 4.861 -8.99 ACEI (-14, -1)) **** **** **** **** 8.99 ACEI (14-day gap) 4.861 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 **** **** SV (14-day gap, history of 7,285 0 **** -10.6 ACEI (-14, -1)) **** **** **** **** **** 10.6 9.880 ACEI (14-day gap) 91 - 180 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 5.748 1.81 -3.5 0.34 (0.08, 1.37) 0.128 ACEI (-14, -1)) **** **** **** **** ACEI (14-day gap) 193.860 5.31 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** 0 SV (14-day gap, history of 3,298 -4.16 **** ACEI (-14, -1)) **** **** **** **** ACEI (14-day gap) 3,298 4.16 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 5.748 **** 1.81 **** -0.82 0.67 (0.12, 3.65) 0.642 ACEI (-14, -1)) **** ACEI (14-day gap) 8,472 2.63

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			Average	Average		Incidence	Risk per	Incidence Rate	Difference in		
		D	_	_	Ni		•			Hazard Ratio	
		Person	Person	Person	Number	Rate per	1,000	Difference per	Risk per		144-1-I
	Number of	Years	Days	Years	of	1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					181 - 270	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	3,659	****	****	****	****	0	****				
ACEI (-14, -1))								-4.87	****	-	-
ACEI (14-day gap)	115,298	****	****	****	****	4.87	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Anal	ysis; Calipe	r= 0.05 ¹							
SV (14-day gap, history of	1,223	****	****	****	****	0	****				
ACEI (-14, -1))	•							-4.95	****	-	-
ACEI (14-day gap)	1,223	****	****	****	****	4.95	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Unco	nditional Ar	alysis; Cali	per= 0.05							
SV (14-day gap, history of	3,661	****	****	****	****	0	****				
ACEI (-14, -1))	•							-8.41	****	-	-
ACEI (14-day gap)	4,853	****	****	****	****	8.41	****				
	·				271 - 365	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	2,588	****	****	****	****	0	****				
ACEI (-14, -1))								-4.21	****	-	-
ACEI (14-day gap)	80,646	****	****	****	****	4.21	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	tional Anal	ysis; Calipe	r= 0.05 ¹							
SV (14-day gap, history of	565	****	****	****	****	0	****				
ACEI (-14, -1))								0	****	-	-
ACEI (14-day gap)	565	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sco		nditional Ar	alysis; Cali	per= 0.05							
SV (14-day gap, history of	2,588	****	****	****	****	0	****				
ACEI (-14, -1))	•							-4.37	****	-	-
ACEI (14-day gap)	3.182	****	****	****	****	4.37	****				
¹Conditional analysis assounts for											

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 30. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	, Risk	Risk	of Events	• '	Users	Years	New Users	` Interval)	P-Value
Age Group: 18-44 Years										·	
Site-Adjusted Analysis											
SV (14-day gap, history of	1,592	****	****	****	****	2.03	****				
ACEI (-14, -1))								-7.12	****	0.22 (0.03, 1.60)	0.136
ACEI (14-day gap)	21,593	****	****	****	****	9.15	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	1,576	****	****	****	****	4.04	****				
ACEI (-14, -1))								-4.04	****	0.50 (0.05, 5.51)	0.571
ACEI (14-day gap)	1,576	****	****	****	****	8.07	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	1,576	****	****	****	****	2.04	****				
ACEI (-14, -1))								-5.55	****	0.27 (0.03, 2.40)	0.239
ACEI (14-day gap)	1,576	****	****	****	****	7.6	****				
Age Group: 45-54 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	3,425	****	****	****	****	3.64	****				
ACEI (-14, -1))								-6.64	****	0.35 (0.13, 0.94)	0.037
ACEI (14-day gap)	45,072	****	****	****	****	10.28	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	3,386	****	****	****	****	6.79	****				
ACEI (-14, -1))								-5.1	****	0.57 (0.17, 1.95)	0.372
ACEI (14-day gap)	3,386	****	****	****	****	11.89	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi		ysis; Calipo	er= 0.05						
SV (14-day gap, history of	3,386	****	****	****	****	3.68	****				
ACEI (-14, -1))								-5.1	****	0.42 (0.13, 1.31)	0.135
ACEI (14-day gap)	3,386	****	****	****	****	8.77	****				

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Table 30. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	. ,	Users	Years	New Users	Interval)	P-Value
Age Group: 55-64 Years	THE COURT			111011	<u> </u>	100.0			11011 00010		1 10100
Site-Adjusted Analysis											
SV (14-day gap, history of	8,067	****	****	****	****	1.58	****				
ACEI (-14, -1))								-7.36	****	0.17 (0.06, 0.46)	< 0.001
ACEI (14-day gap)	97,279	****	****	****	****	8.94	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	8,048	****	****	****	****	2.83	****				
ACEI (-14, -1))								-6.37	****	0.31 (0.10, 0.94)	0.039
ACEI (14-day gap)	8,048	****	****	****	****	9.2	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	8,048	****	****	****	****	1.58	****				
ACEI (-14, -1))								-4.72	****	0.23 (0.08, 0.68)	0.008
ACEI (14-day gap)	8,048	****	****	****	****	6.3	****				
Age Group: 65+ Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	36,545	****	****	****	****	2.52	****				
ACEI (-14, -1))								-3.51	****	0.39 (0.28, 0.56)	<0.001
ACEI (14-day gap)	531,124	****	****	****	****	6.03	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.051						
SV (14-day gap, history of	36,459	****	****	****	****	2.51	****				
ACEI (-14, -1))								-5.44	****	0.32 (0.19, 0.54)	<0.001
ACEI (14-day gap)	36,459	****	****	****	****	7.96	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	36,459	****	****	****	****	2.44	****				
ACEI (-14, -1))								-2.71	****	0.44 (0.29, 0.67)	<0.001
ACEI (14-day gap)	36,459	****	****	****	****	5.15	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 31. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

		Person	Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	NA/al-l
	Number of	Years at	Days at			per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Unknown											
Site-Adjusted Analysis											
SV (14-day gap, history of	8,192	****	****	****	****	1.55	****				
ACEI (-14, -1))								-5.22	****	0.22 (0.08, 0.58)	0.002
ACEI (14-day gap)	99,667	****	****	****	****	6.76	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	8,189	****	****	****	****	1.38	****				
ACEI (-14, -1))								-4.83	****	0.22 (0.05, 1.03)	0.054
ACEI (14-day gap)	8,189	****	****	****	****	6.21	****				
Fixed Ratio 1:1 Propensity So		Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	8,189	****	****	****	****	1.55	****				
ACEI (-14, -1))								-3.39	****	0.30 (0.10, 0.89)	0.03
ACEI (14-day gap)	8,189	****	****	****	****	4.93	****				
Race: American Indian											
Site-Adjusted Analysis											
SV (14-day gap, history of	165	****	****	****	****	0	****				
ACEI (-14, -1))								-2.38	****	-	-
ACEI (14-day gap)	4,526	****	****	****	****	2.38	****				
Fixed Ratio 1:1 Propensity So		Condition	al Analysi	s: Caliper=	0.05						
SV (14-day gap, history of	159	****	****	****	****	0	****				
ACEI (-14, -1))								0	****	-	-
ACEI (14-day gap)	159	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So		Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	159	****	****	****	****	0	****				
ACEI (-14, -1))						-		0	****	-	_
ACEI (14-day gap)	159	****	****	****	****	0	****				

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Table 31. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Asian											
Site-Adjusted Analysis											
SV (14-day gap, history of	526	****	****	****	****	0	****				
ACEI (-14, -1))								-2.63	****	-	-
ACEI (14-day gap)	7,873	****	****	****	****	2.63	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	520	****	****	****	****	0	****				
ACEI (-14, -1))								0	****	-	-
ACEI (14-day gap)	520	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	520	****	****	****	****	0	****				
ACEI (-14, -1))								0	****	-	-
ACEI (14-day gap)	520	****	****	****	****	0	****				
Race: Black											
Site-Adjusted Analysis											
SV (14-day gap, history of	6,074	****	****	****	****	6.91	****				
ACEI (-14, -1))								-15.66	****	0.29 (0.16, 0.51)	<0.001
ACEI (14-day gap)	92,135	****	****	****	****	22.57	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05						
SV (14-day gap, history of	6,067	****	****	****	****	8.07	****				
ACEI (-14, -1))								-19.17	****	0.30 (0.13, 0.65)	0.003
ACEI (14-day gap)	6,067	****	****	****	****	27.24	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	6,067	****	****	****	****	6.92	****				
ACEI (-14, -1))								-10.88	****	0.36 (0.19, 0.69)	0.002
ACEI (14-day gap)	6,067	****	****	****	****	17.8	****				

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Table 31. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ²	Wald P-Value ²
Race: Pacific Islander											
Site-Adjusted Analysis	46	****	****	****	****	0	****				
SV (14-day gap, history of	40					U		-14.36	****	_	_
ACEI (-14, -1))	741	****	****	****	****	14.36	****	-14.50		_	_
ACEI (14-day gap)						14.36					
Fixed Ratio 1:1 Propensity So		****	al Analysis	s; Caliper= ****	****	_	****				
SV (14-day gap, history of	41	****	****	****	****	0	****		****		
ACEI (-14, -1))								0	****	-	-
ACEI (14-day gap)	41	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sc											
SV (14-day gap, history of	41	****	****	****	****	0	****	_			
ACEI (-14, -1))								0	****	-	-
ACEI (14-day gap)	41	****	****	****	****	0	****				
Race: White											
Site-Adjusted Analysis											
SV (14-day gap, history of	34,626	****	****	****	****	2.02	****				
ACEI (-14, -1))								-2.33	****	0.44 (0.30, 0.67)	<0.001
ACEI (14-day gap)	490,126	****	****	****	****	4.35	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	34,613	****	****	****	****	1.58	****				
ACEI (-14, -1))								-4.18	****	0.28 (0.14, 0.54)	< 0.001
ACEI (14-day gap)	34,613	****	****	****	****	5.76	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	34,613	****	****	****	****	2.02	****				
ACEI (-14, -1))								-1.91	****	0.49 (0.30, 0.78)	0.003
ACEI (14-day gap)	34,613	****	****	****	****	3.93	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

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Table 32. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Site-Adjusted Analysis											
SV (14-day gap, history of	35,703	****	****	****	****	3.18	****				
ARBs (-14, -1))								0.16	****	0.99 (0.71, 1.38)	0.937
ARBs (14-day gap)	337,204	****	****	****	****	3.01	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	35,702	****	****	****	****	3.78	****				
ARBs (-14, -1))								1.12	****	1.42 (0.79, 2.56)	0.241
ARBs (14-day gap)	35,702	****	****	****	****	2.66	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	onal Analy	ysis; Calip	er= 0.05						
SV (14-day gap, history of	35,702	****	****	****	****	3.18	****				
ARBs (-14, -1))								0.51	****	1.14 (0.73, 1.77)	0.556
ARBs (14-day gap)	35,702	****	****	****	****	2.67	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 33. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

			Average	Average		Incidence Rate per	Risk per	Incidence Rate	Difference			
		Person	Average Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio		
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald	
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	•	Interval) ²	P-Value ²	
Wedical Floudct	New Osers	at Nisk	at Nisk	at Nisk	Overall	1 Cais	03613	reison rears	New Osers	intervarj	r-value	
Site-Adjusted Analysis												
SV (14-day prior, 14-day gap)	35,703	****	****	****	****	3.18	****	0.15	****	2.22 / 2.71 1.22	0.007	
ARBs (14-day prior, 14-day gap)	337,204	****	****	****	****	3.01	****	0.16	****	0.99 (0.71, 1.38)	0.937	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹								
SV (14-day prior, 14-day gap)	35,702	****	****	****	****	3.78	****	1 12	****	1 42 / 0 70 2 56\	0.241	
ARBs (14-day prior, 14-day gap)	35,702	****	****	****	****	2.66	****	1.12		1.42 (0.79, 2.56)	0.241	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5							
SV (14-day prior, 14-day gap)	35,702	****	****	****	****	3.18	****	0.51	****	1.14 (0.73, 1.77)	0.556	
ARBs (14-day prior, 14-day gap)	35,702	****	****	****	****	2.67	****	0.51		1.14 (0.73, 1.77)	0.550	
					0 - 30 Days	3						
Site-Adjusted Analysis												
SV (14-day prior, 14-day gap)	35,703	****	****	****	****	5.08	****	-0.88	****	0.83 (0.47, 1.45)	0.508	
ARBs (14-day prior, 14-day gap)	337,204	****	****	****	****	5.96	****	0.00		0.03 (0.47, 1.43)	0.500	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹								
SV (14-day prior, 14-day gap)	35,702	****	****	****	****	5.22	****	2.01	****	1.62 (0.67, 3.92)	0.28	
ARBs (14-day prior, 14-day gap)	35,702	****	****	****	****	3.21	****	2.01		1.02 (0.07, 3.92)	0.26	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5							
SV (14-day prior, 14-day gap)	35,702	****	****	****	****	5.08	****	1.22	****	1.28 (0.58, 2.87)	0.542	
ARBs (14-day prior, 14-day gap)	35,702	****	****	****	****	3.86	****	1.22		1.28 (0.38, 2.87)	0.542	
					31 - 60 Day	S						
Site-Adjusted Analysis												
SV (14-day prior, 14-day gap)	26,796	****	****	****	****	3.85	****	0.44	****	1.13 (0.52, 2.45)	0.757	
ARBs (14-day prior, 14-day gap)	316,333	****	****	****	****	3.42	****	0.77		1.13 (0.32, 2.43)	0.757	

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Table 33. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

		Person	Average Person	Average Person		Incidence Rate per 1,000	Risk per 1,000	Incidence Rate Difference	Difference in Risk	Hazard Ratio		
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald	
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²	
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ¹												
SV (14-day prior, 14-day gap)	25,007	****	****	****	****	4.58	****	1.96	****	1.75 (0.51, 5.98)	0.372	
ARBs (14-day prior, 14-day gap)	25,007	****	****	****	****	2.62	****	1.50		1.75 (0.51, 5.56)	0.372	
Fixed Ratio 1:1 Propensity Score	Matched Unco		nalysis; Ca	liper= 0.05	5							
SV (14-day prior, 14-day gap)	26,796	****	****	****	****	3.85	****	1.37	****	1.53 (0.51, 4.54)	0.447	
ARBs (14-day prior, 14-day gap)	33,308	****	****	****	****	2.48	****	1.57		1:55 (0:51, 4:54)	0.447	
					61 - 90 Day	S						
Site-Adjusted Analysis												
SV (14-day prior, 14-day gap)	18,018	****	****	****	****	3.76	****	0.95	****	1.37 (0.55, 3.43)	0.5	
ARBs (14-day prior, 14-day gap)	243,524	****	****	****	****	2.81	****	0.55		1.57 (0.55, 5.45)	0.5	
Fixed Ratio 1:1 Propensity Score	Matched Cond	litional Ana	lysis; Calip	er= 0.05 ¹								
SV (14-day prior, 14-day gap)	13,146	****	****	****	****	2.18	****	1.09	****	2.00 (0.18, 22.06)	0.571	
ARBs (14-day prior, 14-day gap)	13,146	****	****	****	****	1.09	****	1.09		2.00 (0.18, 22.06)	0.571	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5							
SV (14-day prior, 14-day gap)	18,018	****	****	****	****	3.76	****	2.76	****	3.76 (0.73, 19.41)	0.113	
ARBs (14-day prior, 14-day gap)	25,950	****	****	****	****	1	****	2.70		3.70 (0.73, 19.41)	0.113	
				9	1 - 180 Day	rs .						
Site-Adjusted Analysis												
SV (14-day prior, 14-day gap)	14,327	****	****	****	****	2.56	****	0.31	****	1.13 (0.52, 2.45)	0.752	
ARBs (14-day prior, 14-day gap)	214,300	****	****	****	****	2.25	****	0.51		1.13 (0.32, 2.43)	0.752	
Fixed Ratio 1:1 Propensity Score	Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ¹											
SV (14-day prior, 14-day gap)	9,233	****	****	****	****	3.04	****	-0.76	****	0.80 (0.21, 2.98)	0.739	
ARBs (14-day prior, 14-day gap)	9,233	****	****	****	****	3.8	****	-0.76		0.00 (0.21, 2.98)	0.733	

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Table 33. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time

						Incidence		Incidence			
			Average	Average		Rate per	Risk per	Rate	Difference		
		Person	Person	Person		1,000	1,000	Difference	in Risk	Hazard Ratio	
	Number of	Years	Days	Years	Number	Person	New	per 1,000	per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	of Events	Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05							
SV (14-day prior, 14-day gap)	14,327	****	****	****	****	2.56	****	-1.58	****	0.62 (0.26, 1.49)	0.284
ARBs (14-day prior, 14-day gap)	22,771	****	****	****	****	4.14	****	-1.56		0.02 (0.20, 1.49)	0.264
				18	81 - 270 Da	ys					
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	9,006	****	****	****	****	1.63	****	-0.44	****	0.80 (0.25, 2.57)	0.714
ARBs (14-day prior, 14-day gap)	130,102	****	****	****	****	2.07	****	-0.44		0.80 (0.25, 2.57)	0.714
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (14-day prior, 14-day gap)	3,388	****	****	****	****	0	****	0	****		_
ARBs (14-day prior, 14-day gap)	3,388	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (14-day prior, 14-day gap)	9,006	****	****	****	****	1.63	****	-0.21	****	0.87 (0.21, 3.66)	0.854
ARBs (14-day prior, 14-day gap)	13,456	****	****	****	****	1.84	****	-0.21		0.87 (0.21, 3.00)	0.654
				27	71 - 365 Da	ys					
Site-Adjusted Analysis											
SV (14-day prior, 14-day gap)	6,275	****	****	****	****	1.47	****	-0.09	****	0.97 (0.23, 4.03)	0.962
ARBs (14-day prior, 14-day gap)	92,658	****	****	****	****	1.56	****	-0.09		0.97 (0.23, 4.03)	0.902
Fixed Ratio 1:1 Propensity Score	Matched Cond	itional Ana	lysis; Calip	er= 0.05 ¹							
SV (14-day prior, 14-day gap)	1,660	****	****	****	****	3.26	****	0	****	1.00 (0.06, 15.99)	1
ARBs (14-day prior, 14-day gap)	1,660	****	****	****	****	3.26	****			1.00 (0.00, 13.99)	
Fixed Ratio 1:1 Propensity Score	Matched Unco	nditional A	nalysis; Ca	liper= 0.05	5						
SV (14-day prior, 14-day gap)	6,275	****	****	****	****	1.47	****	0.48	****	1.48 (0.21, 10.48)	0.697
ARBs (14-day prior, 14-day gap)	9,317	****	****	****	****	0.99	****	0.46		1.40 (0.21, 10.46)	0.037

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

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Table 34. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	· Interval)²	P-Value ²
No Angioedema (-183, -1)	11011 00010		11.011		0. 2. 00	1.00.10					
Site-Adjusted Analysis											
SV (14-day gap, history of	35,668	****	****	****	****	2.84	****				
ARBs (-14, -1))								0.4	****	1.12 (0.78, 1.59)	0.546
ARBs (14-day gap)	336,379	****	****	****	****	2.43	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	35,667	****	****	****	****	3.23	****				,
ARBs (-14, -1))								0.98	****	1.44 (0.76, 2.72)	0.265
ARBs (14-day gap)	35,667	****	****	****	****	2.24	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	35,667	****	****	****	****	2.84	****				
ARBs (-14, -1))								0.41	****	1.14 (0.71, 1.81)	0.591
ARBs (14-day gap)	35,667	****	****	****	****	2.42	****				
Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	35	****	****	****	****	390.63	****				
ARBs (-14, -1))								118.99	****	1.30 (0.48, 3.57)	0.605
ARBs (14-day gap)	825	****	****	****	****	271.63	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	33	****	****	****	****	776.7	****				
ARBs (-14, -1))								776.7	****	-	-
ARBs (14-day gap)	33	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Se	ore Matched	Unconditi	onal Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	33	****	****	****	****	439.08	****				
ARBs (-14, -1))								330.56	****	2.84 (0.51, 15.71)	0.233
ARBs (14-day gap)	33	****	****	****	****	108.52	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

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Table 35. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)

	Number of	Person Years at	Average Person Days at	Person	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	Interval)	P-Value
No Angioedema (ever, -1)										,	
Site-Adjusted Analysis											
SV (14-day gap, history of	35,162	****	****	****	****	2.53	****				
ARBs (-14, -1))								0.49	****	1.19 (0.81, 1.74)	0.369
ARBs (14-day gap)	329,845	****	****	****	****	2.03	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	35,157	****	****	****	****	2.85	****				,
ARBs (-14, -1))								1.14	****	1.67 (0.81, 3.41)	0.162
ARBs (14-day gap)	35,157	****	****	****	****	1.71	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	35,157	****	****	****	****	2.53	****				
ARBs (-14, -1))								0.63	****	1.29 (0.77, 2.15)	0.329
ARBs (14-day gap)	35,157	****	****	****	****	1.89	****				
Angioedema (ever, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	541	****	****	****	****	49.9	****				
ARBs (-14, -1))								1.96	****	0.87 (0.43, 1.78)	0.705
ARBs (14-day gap)	7,359	****	****	****	****	47.94	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	535	****	****	****	****	81.05	****				
ARBs (-14, -1))								30.39	****	1.60 (0.52, 4.89)	0.41
ARBs (14-day gap)	535	****	****	****	****	50.65	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	535	****	****	****	****	50.8	****				
ARBs (-14, -1))								13.01	****	1.20 (0.46, 3.14)	0.706
ARBs (14-day gap)	535	****	****	****	****	37.79	****				

¹Conditional analysis accounts for informative events and person-time.

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Table 36. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies

	Number of	Person Years at	Average Person	Person	Nivenhau	Incidence Rate	Risk per 1,000 New	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	Wald
Medical Product	New Users	Risk	Days at Risk	Risk	of Events	per 1,000 Person		1,000 Person	1,000 New Users	(95% Confidence	
	New Osers	RISK	RISK	RISK	or Events	Years	Users	Years	New Osers	Interval)	P-Value
No Serious allergies Site-Adjusted Analysis											
	21 221	****	****	****	****	2.8	****				
SV (14-day gap, history of	31,231					2.8		0.22	****	1.02 (0.70, 1.49)	0.925
ARBs (-14, -1))	202 750	****	****	****	****	2.50	****	0.22		1.02 (0.70, 1.49)	0.323
ARBs (14-day gap)	282,750					2.59					
Fixed Ratio 1:1 Propensity So											
SV (14-day gap, history of	31,227	****	****	****	****	3.32	****				
ARBs (-14, -1))								0.47	****	1.17 (0.62, 2.19)	0.631
ARBs (14-day gap)	31,227	****	****	****	****	2.85	****				
Fixed Ratio 1:1 Propensity So	ore Matched										
SV (14-day gap, history of	31,227	****	****	****	****	2.8	****				
ARBs (-14, -1))								0.12	****	0.99 (0.61, 1.61)	0.975
ARBs (14-day gap)	31,227	****	****	****	****	2.68	****				
Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	4,472	****	****	****	****	6.14	****				
ARBs (-14, -1))								0.65	****	1.03 (0.50, 2.11)	0.931
ARBs (14-day gap)	54,454	****	****	****	****	5.5	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	4,459	****	****	****	****	6.37	****				
ARBs (-14, -1))	,							5.09	****	5.00 (0.58, 42.80)	0.142
ARBs (14-day gap)	4,459	****	****	****	****	1.27	****			, , ,	
Fixed Ratio 1:1 Propensity So		Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	4,459	****	****	****	****	6.16	****				
ARBs (-141))	.,							2.81	****	1.80 (0.62, 5.21)	0.278
ARBs (14-day gap)	4,459	****	****	****	****	3.36	****			, , ,	
(= . ~~1 0~~)	.,					0.00					

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



		Person	Average Person	Average Person	Number	Incidence	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
Sex: Male											
					Overa	II					
Site-Adjusted Analysis											
SV (14-day gap, history of	21,802	****	****	****	****	2.21	****				
ARBs (-14, -1))								-0.69	****	0.72 (0.43, 1.20)	0.206
ARBs (14-day gap)	149,279	****	****	****	****	2.9	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	21,792	****	****	****	****	2.74	****				
ARBs (-14, -1))								0.46	****	1.20 (0.52, 2.78)	0.67
ARBs (14-day gap)	21,792	****	****	****	****	2.29	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Calip	oer= 0.05							
SV (14-day gap, history of	21,792	****	****	****	****	2.21	****				
ARBs (-14, -1))								-0.37	****	0.81 (0.43, 1.53)	0.519
ARBs (14-day gap)	21,792	****	****	****	****	2.58	****				
					0 - 30 D	ays					
Site-Adjusted Analysis											
SV (14-day gap, history of	21,802	****	****	****	****	5.1	****				
ARBs (-14, -1))								0.08	****	0.97 (0.46, 2.03)	0.941
ARBs (14-day gap)	149,279	****	****	****	****	5.02	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	21,792	****	****	****	****	5.27	****				
ARBs (-14, -1))								1.98	****	1.60 (0.52, 4.89)	0.41
ARBs (14-day gap)	21,792	****	****	****	****	3.29	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor										
SV (14-day gap, history of	21,792	****	****	****	****	5.11	****				
ARBs (-14, -1))								1.64	****	1.43 (0.50, 4.12)	0.509
ARBs (14-day gap)	21,792	****	****	****	****	3.47	****				

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Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed

Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time **Incidence Rate** Difference Average Average Risk per **Hazard Ratio** Person Person Number Incidence 1.000 Difference per in Risk per Person (95% Confidence Wald Number of Years Years of Rate per 1,000 New 1.000 1.000 Days **Medical Product** Interval)2 P-Value² **New Users** at Risk at Risk at Risk **Events Person Years** Users **Person Years New Users** 31 - 60 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 16,532 1.78 0.61 (0.14, 2.54) -1.1 0.493 ARBs (-14, -1)) **** **** **** **** 139.809 2.88 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** **** **** SV (14-day gap, history of 15.257 2.13 1.07 2.00 (0.18, 22.06) 0.571 ARBs (-14, -1)) **** **** **** **** **** 1.07 ARBs (14-day gap) 15,257 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 **** **** SV (14-day gap, history of 16,525 1.78 -0.96 0.65 (0.12, 3.54) 0.616 ARBs (-14, -1)) **** **** **** **** **** 2.74 20.080 ARBs (14-day gap) 61 - 90 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 11.206 2.42 0.01 1.03 (0.24, 4.41) 0.968 ARBs (-14, -1)) **** **** **** **** ARBs (14-day gap) 107.362 2.41 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** 1.77 SV (14-day gap, history of 8,113 1.77 **** ARBs (-14, -1)) **** **** **** **** **** 8,113 0 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 11.204 **** 2.42 ****

0

2.42

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ARBs (-14, -1))

ARBs (14-day gap)

15,670



Incidence Rate Difference Average Average Risk per **Hazard Ratio** Person Person Number Incidence 1.000 Difference per in Risk per Person (95% Confidence Wald Number of Years Years of Rate per 1,000 New 1.000 1.000 Days **Medical Product** Interval)2 P-Value² **New Users** at Risk at Risk at Risk **Events Person Years** Users **Person Years New Users** 91 - 180 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 8,904 1.76 -1 0.63 (0.19, 2.01) 0.431 ARBs (-14, -1)) **** **** **** **** 94.229 2.76 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** **** **** SV (14-day gap, history of 5.669 1.24 -2.480.33 (0.03, 3.20) 0.341 ARBs (-14, -1)) **** **** **** **** **** 5.669 3.72 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 **** **** SV (14-day gap, history of 8,901 1.76 -2.7 0.39 (0.11, 1.40) 0.149 ARBs (-14, -1)) **** **** **** **** **** 4.46 13,656 ARBs (14-day gap) 181 - 270 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 5.643 0.87 -0.96 0.50 (0.07, 3.69) 0.493 ARBs (-14, -1)) **** **** **** **** ARBs (14-day gap) 56.419 1.83 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** 0 SV (14-day gap, history of 2,082 0 **** ARBs (-14, -1)) **** **** **** **** **** 2,082 0 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 5.641 **** 0.87 **** -0.98 0.46 (0.05, 4.40) 0.498 ARBs (-14, -1)) **** ARBs (14-day gap) 8.063 1.85

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, , ,	•		Average	Average		•	Risk per	Incidence Rate	Difference		
		Person	Person	Person	Number	Incidence	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					271 - 365	Days				,	
Site-Adjusted Analysis						·					
SV (14-day gap, history of	3,939	****	****	****	****	0	****				
ARBs (-14, -1))								-2.15	****	-	-
ARBs (14-day gap)	39,965	****	****	****	****	2.15	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi	itional Analy	ysis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	1,043	****	****	****	****	0	****				
ARBs (-14, -1))								-5.18	****	-	-
ARBs (14-day gap)	1,043	****	****	****	****	5.18	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Unco	nditional An	alysis; Cali _l	per= 0.05							
SV (14-day gap, history of	3,939	****	****	****	****	0	****				
ARBs (-14, -1))								-0.84	****	-	-
ARBs (14-day gap)	5,566	****	****	****	****	0.84	****				
Sex: Female											
					Overa	II					
Site-Adjusted Analysis											
SV (14-day gap, history of	13,901	****	****	****	****	4.77	****				
ARBs (-14, -1))								1.66	****	1.42 (0.91, 2.21)	0.125
ARBs (14-day gap)	187,925	****	****	****	****	3.1	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Condi										
SV (14-day gap, history of	13,901	****	****	****	****	5.57	****				
ARBs (-14, -1))								2.6	****	1.87 (0.79, 4.42)	0.151
ARBs (14-day gap)	13,901	****	****	****	****	2.97	****				
Fixed Ratio 1:1 Propensity Sco	re Matched Unco		•								
SV (14-day gap, history of	13,901	****	****	****	****	4.77	****				
ARBs (-14, -1))								1.86	****	1.59 (0.85, 3.00)	0.148
ARBs (14-day gap)	13,901	****	****	****	****	2.9	****				

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Incidence Rate Difference Average Average Risk per **Hazard Ratio** Person Number Incidence 1.000 Difference per in Risk per Person Person (95% Confidence Wald Number of Years Years of Rate per 1,000 New 1.000 1.000 Days **Medical Product** Interval)2 P-Value² **New Users** at Risk at Risk at Risk **Events Person Years** Users **Person Years New Users** 0 - 30 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 13,901 5.05 -1.65 0.73 (0.30, 1.80) 0.501 ARBs (-14, -1)) **** **** **** **** 187.925 6.71 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** **** **** SV (14-day gap, history of 13.901 5.2 0 1.00 (0.29, 3.45) 1 ARBs (-14, -1)) **** **** **** **** **** 13,901 5.2 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 **** **** SV (14-day gap, history of 13,901 5.05 -0.36 0.92 (0.28, 3.00) 0.885 ARBs (-14, -1)) **** **** **** **** **** 5.42 13.901 ARBs (14-day gap) 31 - 60 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 10.264 7.23 3.39 1.88 (0.75, 4.72) 0.178 ARBs (-14, -1)) **** **** **** **** ARBs (14-day gap) 176,524 3.84 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** SV (14-day gap, history of 9,530 8.68 6.94 5.00 (0.58, 42.80) 0.142 ARBs (-14, -1)) **** **** **** **** **** 9,530 1.74 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 10.264 **** 7.23 **** 6.16 6.54 (0.76, 56.04) 0.086 ARBs (-14, -1)) **** ARBs (14-day gap) 12,900 1.07

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Incidence Rate Difference Average Average Risk per **Hazard Ratio** Person Person Number Incidence 1.000 Difference per in Risk per Person (95% Confidence Wald Number of Years Years of Rate per 1,000 New 1.000 1.000 Days **Medical Product** Interval)2 P-Value² **New Users** at Risk at Risk at Risk **Events Person Years** Users **Person Years New Users** 61 - 90 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 6,812 5.97 2.84 1.95 (0.60, 6.35) 0.269 ARBs (-14, -1)) **** **** **** **** 136.162 3.13 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** **** **** SV (14-day gap, history of 4.891 2.92 0 1.00 (0.06, 15.99) 1 ARBs (-14, -1)) **** **** **** **** **** 2.92 ARBs (14-day gap) 4.891 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 **** **** SV (14-day gap, history of 6,812 5.97 3.37 2.30 (0.38, 13.78) 0.361 ARBs (-14, -1)) **** **** **** **** **** 2.59 9.983 ARBs (14-day gap) 91 - 180 Days **Site-Adjusted Analysis** **** **** **** **** **** SV (14-day gap, history of 5,423 3.88 2.02 2.13 (0.76, 5.96) 0.148 ARBs (-14, -1)) **** **** **** **** ARBs (14-day gap) 120,071 1.86 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ **** **** SV (14-day gap, history of 3,431 6.16 4.11 3.00 (0.31, 28.84) 0.341 ARBs (-14, -1)) **** **** **** **** **** 3,431 2.05 ARBs (14-day gap) Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 5.423 **** 3.88 **** 0.07 1.03 (0.29, 3.64) 0.969 ARBs (-14, -1)) **** ARBs (14-day gap) 8.740 3.81

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		Person	Average Person	Average Person	Number	Incidence	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Rate per 1,000	New	1,000	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Person Years	Users	Person Years	New Users	Interval) ²	P-Value ²
					181 - 270	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	3,363	****	****	****	****	2.92	****				
ARBs (-14, -1))								0.67	****	1.31 (0.32, 5.47)	0.708
ARBs (14-day gap)	73,683	****	****	****	****	2.25	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	1,256	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	1,256	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	oer= 0.05							
SV (14-day gap, history of	3,363	****	****	****	****	2.92	****				
ARBs (-14, -1))								1	****	1.54 (0.22, 10.93)	0.666
ARBs (14-day gap)	5,149	****	****	****	****	1.92	****				
					271 - 365	Days					
Site-Adjusted Analysis											
SV (14-day gap, history of	2,336	****	****	****	****	3.95	****				
ARBs (-14, -1))								2.84	****	3.91 (0.88, 17.36)	0.073
ARBs (14-day gap)	52,693	****	****	****	****	1.11	****				
Fixed Ratio 1:1 Propensity Score	Matched Condi	tional Analy	sis; Caliper	= 0.05 ¹							
SV (14-day gap, history of	618	****	****	****	****	8.8	****				
ARBs (-14, -1))								8.8	****	-	-
ARBs (14-day gap)	618	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score	Matched Uncor	nditional An	alysis; Cali	per= 0.05							
SV (14-day gap, history of	2,337	****	****	****	****	3.95	****				
ARBs (-14, -1))								2.66	****	3.08 (0.28, 33.93)	0.359
ARBs (14-day gap)	3,560	****	****	****	****	1.28	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 38. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
Age Group: 18-44 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	774	****	****	****	****	0	****				
ARBs (-14, -1))								-7.89	****	-	-
ARBs (14-day gap)	8,505	****	****	****	****	7.89	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	762	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	762	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	762	****	****	****	****	0	****				
ARBs (-14, -1))								-4.13	****	-	-
ARBs (14-day gap)	762	****	****	****	****	4.13	****				
Age Group: 45-54 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	1,794	****	****	****	****	3.8	****				
ARBs (-14, -1))								-0.52	****	0.88 (0.21, 3.71)	0.866
ARBs (14-day gap)	18,304	****	****	****	****	4.32	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	1,786	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	1,786	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	1,786	****	****	****	****	3.81	****				
ARBs (-14, -1))								2.31	****	2.49 (0.23, 27.53)	0.456
ARBs (14-day gap)	1,786	****	****	****	****	1.5	****				

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Table 38. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Age Group: 55-64 Years	iteli Oseis	MISK	MISK	TUSK	OI EVEITES	16415	03613	16013	itew osers	intervaly	· value
Site-Adjusted Analysis											
SV (14-day gap, history of	4,275	****	****	****	****	6.8	****				
ARBs (-14, -1))	•							2.8	****	1.62 (0.81, 3.27)	0.173
ARBs (14-day gap)	40,567	****	****	****	****	3.99	****			, , ,	
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	4,246	****	****	****	****	9.29	****				
ARBs (-14, -1))	•							6.64	****	3.50 (0.73, 16.85)	0.118
ARBs (14-day gap)	4,246	****	****	****	****	2.66	****				
Fixed Ratio 1:1 Propensity S	core Matched	Unconditi	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	4,246	****	****	****	****	6.83	****				
ARBs (-14, -1))								4.46	****	2.68 (0.83, 8.74)	0.101
ARBs (14-day gap)	4,246	****	****	****	****	2.37	****				
Age Group: 65+ Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	28,860	****	****	****	****	2.72	****				
ARBs (-14, -1))								0.02	****	0.94 (0.63, 1.40)	0.747
ARBs (14-day gap)	269,828	****	****	****	****	2.71	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	28,797	****	****	****	****	3.24	****				
ARBs (-14, -1))								0.17	****	1.06 (0.55, 2.01)	0.869
ARBs (14-day gap)	28,797	****	****	****	****	3.07	****				
Fixed Ratio 1:1 Propensity S	core Matched	Unconditi	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	28,797	****	****	****	****	2.73	****				
ARBs (-14, -1))								-0.14	****	0.91 (0.55, 1.50)	0.705
ARBs (14-day gap)	28,797	****	****	****	****	2.87	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 39. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	· Interval) ²	P-Value ²
Race: Unknown	11011 00010	11.011	11.011		0. 2. 0. 1. 0.				11011 00010		1 10.00
Site-Adjusted Analysis											
SV (14-day gap, history of	5,777	****	****	****	****	2.23	****				
ARBs (-14, -1))	•							-0.28	****	0.85 (0.31, 2.35)	0.751
ARBs (14-day gap)	47,811	****	****	****	****	2.51	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	5,748	****	****	****	****	3.87	****				
ARBs (-14, -1))	•							1.93	****	2.00 (0.37, 10.92)	0.423
ARBs (14-day gap)	5,748	****	****	****	****	1.93	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	5,748	****	****	****	****	2.24	****				
ARBs (-14, -1))								-2.31	****	0.48 (0.15, 1.50)	0.205
ARBs (14-day gap)	5,748	****	****	****	****	4.55	****				
Race: American Indian											
Site-Adjusted Analysis											
SV (14-day gap, history of	86	****	****	****	****	0	****				
ARBs (-14, -1))								-1.36	****	-	-
ARBs (14-day gap)	1,948	****	****	****	****	1.36	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	83	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	83	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	83	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	83	****	****	****	****	0	****				

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Table 39. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Asian											
Site-Adjusted Analysis											
SV (14-day gap, history of	863	****	****	****	****	0	****				
ARBs (-14, -1))								-0.81	****	-	-
ARBs (14-day gap)	7,814	****	****	****	****	0.81	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	834	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	834	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	834	****	****	****	****	0	****				
ARBs (-14, -1))								-2.55	****	-	-
ARBs (14-day gap)	834	****	****	****	****	2.55	****				
Race: Black											
Site-Adjusted Analysis											
SV (14-day gap, history of	4,832	****	****	****	****	4.4	****				
ARBs (-14, -1))								-2.4	****	0.60 (0.27, 1.36)	0.222
ARBs (14-day gap)	55,825	****	****	****	****	6.8	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.051						
SV (14-day gap, history of	4,829	****	****	****	****	4.93	****				
ARBs (-14, -1))								-3.7	****	0.57 (0.17, 1.95)	0.372
ARBs (14-day gap)	4,829	****	****	****	****	8.62	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	4,829	****	****	****	****	4.4	****				
ARBs (-14, -1))								-0.4	****	0.82 (0.29, 2.31)	0.704
ARBs (14-day gap)	4,829	****	****	****	****	4.8	****				

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Table 39. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Person		Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Pacific Islander											
Site-Adjusted Analysis											
SV (14-day gap, history of	46	****	****	****	****	0	****				
ARBs (-14, -1))								-8.97	****	-	-
ARBs (14-day gap)	478	****	****	****	****	8.97	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	40	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	40	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	40	****	****	****	****	0	****				
ARBs (-14, -1))								0	****	-	-
ARBs (14-day gap)	40	****	****	****	****	0	****				
Race: White											
Site-Adjusted Analysis											
SV (14-day gap, history of	24,099	****	****	****	****	3.29	****				
ARBs (-14, -1))								0.89	****	1.28 (0.86, 1.90)	0.229
ARBs (14-day gap)	223,328	****	****	****	****	2.4	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	24,091	****	****	****	****	3.56	****				
ARBs (-14, -1))	•							0.99	****	1.38 (0.68, 2.83)	0.371
ARBs (14-day gap)	24,091	****	****	****	****	2.57	****			, . ,	
Fixed Ratio 1:1 Propensity So		Unconditi	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	24,091	****	****	****	****	3.3	****				
ARBs (-14, -1))	•							1.24	****	1.55 (0.89, 2.70)	0.124
ARBs (14-day gap)	24,091	****	****	****	****	2.06	****			•	
1	,										

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 40. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Site-Adjusted Analysis											
SV (7-day gap, history of	69,639	****	****	****	****	2.14	****				
ACEI (-183, -1))								-4.77	****	0.29 (0.21, 0.39)	<0.001
ACEI (7-day gap)	694,882	****	****	****	****	6.91	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (7-day gap, history of	69,639	****	****	****	****	2.84	****				
ACEI (-183, -1))								-8.42	****	0.25 (0.17, 0.37)	< 0.001
ACEI (7-day gap)	69,639	****	****	****	****	11.26	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	onal Analy	ysis; Calipo	er= 0.05						
SV (7-day gap, history of	69,639	****	****	****	****	2.14	****	_		_	
ACEI (-183, -1))								-4.48	****	0.30 (0.21, 0.41)	< 0.001
ACEI (7-day gap)	69,639	****	****	****	****	6.62	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 41. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Person	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Site-Adjusted Analysis											
SV (7-day gap, history of	49,140	****	****	****	****	2.85	****				
ARBs (-183, -1))								-0.19	****	0.87 (0.63, 1.20)	0.388
ARBs (7-day gap)	337,083	****	****	****	****	3.04	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (7-day gap, history of	49,137	****	****	****	****	3.48	****				
ARBs (-183, -1))								0	****	1.00 (0.60, 1.66)	1
ARBs (7-day gap)	49,137	****	****	****	****	3.48	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	onal Analy	ysis; Calipo	er= 0.05						
SV (7-day gap, history of	49,137	****	****	****	****	2.85	****	_		_	
ARBs (-183, -1))								-0.1	****	0.91 (0.61, 1.35)	0.626
ARBs (7-day gap)	49,137	****	****	****	****	2.95	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 42. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Site-Adjusted Analysis											
SV (14-day gap, history of	69,639	****	****	****	****	0.86	****				
ACEI (-183, -1))								-1.14	****	0.42 (0.27, 0.64)	<0.001
ACEI (14-day gap)	694,882	****	****	****	****	2	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	69,639	****	****	****	****	1.07	****				
ACEI (-183, -1))								-1.93	****	0.36 (0.20, 0.64)	< 0.001
ACEI (14-day gap)	69,639	****	****	****	****	3	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Analy	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	69,639	****	****	****	****	0.86	****				
ACEI (-183, -1))								-0.99	****	0.44 (0.27, 0.73)	0.001
ACEI (14-day gap)	69,639	****	****	****	****	1.86	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 43. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)

			Average	Average			Risk per	Incidence Rate	Difference		
		Person	Person	Person		Incidence Rate	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at	Number	per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
No Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	69,556	****	****	****	****	0.82	****				
ACEI (-183, -1))								-1.1	****	0.41 (0.26, 0.65)	< 0.001
ACEI (14-day gap)	694,018	****	****	****	****	1.93	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	69,556	****	****	****	****	1	****				
ACEI (-183, -1))								-1.86	****	0.35 (0.19, 0.64)	< 0.001
ACEI (14-day gap)	69,556	****	****	****	****	2.86	****				
Fixed Ratio 1:1 Propensity S	core Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	69,556	****	****	****	****	0.82	****				
ACEI (-183, -1))								-0.97	****	0.44 (0.26, 0.73)	0.002
ACEI (14-day gap)	69,556	****	****	****	****	1.79	****				
Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	83	****	****	****	****	34.92	****				
ACEI (-183, -1))								-40.45	****	0.54 (0.07, 4.00)	0.547
ACEI (14-day gap)	864	****	****	****	****	75.37	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	• 0.05 ¹						
SV (14-day gap, history of	68	****	****	****	****	80.52	****				
ACEI (-183, -1))								0	****	1.00 (0.06, 15.99)	1
ACEI (14-day gap)	68	****	****	****	****	80.52	****				
Fixed Ratio 1:1 Propensity S	core Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	68	****	****	****	****	43.22	****				
ACEI (-183, -1))								-4.54	****	1.06 (0.07, 16.94)	0.967
ACEI (14-day gap)	68	****	****	****	****	47.76	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 44. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)

			Average	Average			Risk per	Incidence Rate	Difference		
		Person	Person	Person		Incidence Rate	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at	Number	per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
No Angioedema (ever, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	69,145	****	****	****	****	0.83	****				
ACEI (-183, -1))								-0.92	****	0.46 (0.29, 0.72)	< 0.001
ACEI (14-day gap)	687,565	****	****	****	****	1.75	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	69,144	****	****	****	****	1.01	****				
ACEI (-183, -1))								-1.58	****	0.39 (0.21, 0.72)	0.003
ACEI (14-day gap)	69,144	****	****	****	****	2.59	****				
Fixed Ratio 1:1 Propensity S	core Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	69,144	****	****	****	****	0.83	****				
ACEI (-183, -1))								-0.77	****	0.49 (0.29, 0.84)	0.009
ACEI (14-day gap)	69,144	****	****	****	****	1.59	****				
Angioedema (ever, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	494	****	****	****	****	6.3	****				
ACEI (-183, -1))								-22.43	****	0.22 (0.03, 1.56)	0.128
ACEI (14-day gap)	7,317	****	****	****	****	28.73	****				
Fixed Ratio 1:1 Propensity S	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	487	****	****	****	****	11.83	****				
ACEI (-183, -1))								-23.66	****	0.33 (0.03, 3.20)	0.341
ACEI (14-day gap)	487	****	****	****	****	35.49	****				
Fixed Ratio 1:1 Propensity S	core Matched	Uncondit	ional Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	487	****	****	****	****	6.38	****				
ACEI (-183, -1))								-16.84	****	0.28 (0.03, 2.48)	0.251
ACEI (14-day gap)	487	****	****	****	****	23.22	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 45. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies

,			Average	Average	,		Risk per	Incidence Rate	Difference	••	
		Person	Person	Person		Incidence Rate	1,000	Difference per	in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at	Number	per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
No Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	61,592	****	****	****	****	0.83	****				
ACEI (-183, -1))								-1.02	****	0.43 (0.27, 0.69)	<0.001
ACEI (14-day gap)	583,922	****	****	****	****	1.85	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.051						
SV (14-day gap, history of	61,582	****	****	****	****	0.96	****				
ACEI (-183, -1))								-1.52	****	0.39 (0.20, 0.75)	0.005
ACEI (14-day gap)	61,582	****	****	****	****	2.48	****				
Fixed Ratio 1:1 Propensity So			ional Anal								
SV (14-day gap, history of	61,582	****	****	****	****	0.83	****				
ACEI (-183, -1))								-0.8	****	0.48 (0.28, 0.84)	0.01
ACEI (14-day gap)	61,582	****	****	****	****	1.63	****				
Serious allergies											
Site-Adjusted Analysis											
SV (14-day gap, history of	8,047	****	****	****	****	1.15	****		ale ale ale ale ale		
ACEI (-183, -1))								-1.77	****	0.39 (0.12, 1.22)	0.105
ACEI (14-day gap)	110,960	****	****	****	****	2.92	*****				
Fixed Ratio 1:1 Propensity So	ore Matched										
SV (14-day gap, history of	8,038	****	****	****	****	1.38	****				
ACEI (-183, -1))								-3.45	****	0.29 (0.06, 1.38)	0.118
ACEI (14-day gap)	8,038	****	****	****	****	4.84	****				
Fixed Ratio 1:1 Propensity So											
SV (14-day gap, history of	8,038	****	****	****	****	1.15	****			,	
ACEI (-183, -1))								-1.88	****	0.37 (0.10, 1.36)	0.135
ACEI (14-day gap)	8,038	****	****	****	****	3.03	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 46. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Sex

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Sex: Male										, i	
Site-Adjusted Analysis											
SV (14-day gap, history of	48,440	****	****	****	****	1	****				
ACEI (-183, -1))								-0.58	****	0.60 (0.37, 0.99)	0.044
ACEI (14-day gap)	353,015	****	****	****	****	1.57	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	48,398	****	****	****	****	1.02	****				
ACEI (-183, -1))								-1.13	****	0.48 (0.22, 1.01)	0.053
ACEI (14-day gap)	48,398	****	****	****	****	2.15	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	48,398	****	****	****	****	1	****				
ACEI (-183, -1))								-0.44	****	0.66 (0.36, 1.19)	0.166
ACEI (14-day gap)	48,398	****	****	****	****	1.43	****				
Sex: Female											
Site-Adjusted Analysis											
SV (14-day gap, history of	21,199	****	****	****	****	0.55	****				
ACEI (-183, -1))								-1.9	****	0.22 (0.08, 0.59)	0.002
ACEI (14-day gap)	341,867	****	****	****	****	2.45	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	21,198	****	****	****	****	0.74	****				
ACEI (-183, -1))								-2.22	****	0.25 (0.07, 0.89)	0.032
ACEI (14-day gap)	21,198	****	****	****	****	2.96	****				
Fixed Ratio 1:1 Propensity Se	core Matched	Unconditi	onal Anal	ysis; Calip	er= 0.05						
SV (14-day gap, history of	21,198	****	****	****	****	0.55	****				
ACEI (-183, -1))								-1.32	****	0.28 (0.09, 0.85)	0.024
ACEI (14-day gap)	21,198	****	****	****	****	1.87	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 47. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Average Person Days at	Person Years at		Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Age Group: 18-44 Years											
Site-Adjusted Analysis		****	****	****	****		****				
SV (14-day gap, history of	2,412	****	****	****	****	0	****	2.26	****		
ACEI (-183, -1))								-3.36	****	-	-
ACEI (14-day gap)	21,587	****	****	****	****	3.36	****				
Fixed Ratio 1:1 Propensity So	ore Matched		al Analysi		: 0.05 ¹						
SV (14-day gap, history of	2,385	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	2,385	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched		ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	2,385	****	****	****	****	0	****				
ACEI (-183, -1))								-1.24	****	-	-
ACEI (14-day gap)	2,385	****	****	****	****	1.24	****				
Age Group: 45-54 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	5,115	****	****	****	****	1.17	****				
ACEI (-183, -1))								-1.62	****	0.45 (0.11, 1.84)	0.264
ACEI (14-day gap)	45,057	****	****	****	****	2.79	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	5,075	****	****	****	****	1.09	****				
ACEI (-183, -1))								-1.09	****	0.50 (0.05, 5.51)	0.571
ACEI (14-day gap)	5,075	****	****	****	****	2.17	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	5,075	****	****	****	****	1.18	****				
ACEI (-183, -1))								-0.43	****	0.68 (0.11, 4.05)	0.669
ACEI (14-day gap)	5,075	****	****	****	****	1.61	****				

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Table 47. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Average Person Days at	Person	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1.000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	•	Users	Years	New Users	Interval) ²	P-Value ²
Age Group: 55-64 Years										,	
Site-Adjusted Analysis											
SV (14-day gap, history of	11,494	****	****	****	****	1.83	****				
ACEI (-183, -1))								-1.41	****	0.57 (0.27, 1.22)	0.148
ACEI (14-day gap)	97,244	****	****	****	****	3.25	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	11,435	****	****	****	****	1.88	****				
ACEI (-183, -1))								-4.22	****	0.31 (0.10, 0.94)	0.039
ACEI (14-day gap)	11,435	****	****	****	****	6.1	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	11,435	****	****	****	****	1.84	****				
ACEI (-183, -1))								-2.15	****	0.45 (0.19, 1.07)	0.071
ACEI (14-day gap)	11,435	****	****	****	****	4	****				
Age Group: 65+ Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	50,618	****	****	****	****	0.67	****				
ACEI (-183, -1))								-1.03	****	0.38 (0.21, 0.67)	<0.001
ACEI (14-day gap)	530,994	****	****	****	****	1.69	****				
Fixed Ratio 1:1 Propensity So	core Matched		al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	50,470	****	****	****	****	0.77	****				
ACEI (-183, -1))								-1.53	****	0.33 (0.15, 0.74)	0.007
ACEI (14-day gap)	50,470	****	****	****	****	2.3	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	ional Anal		er= 0.05						
SV (14-day gap, history of	50,470	****	****	****	****	0.67	****				
ACEI (-183, -1))								-0.63	****	0.48 (0.24, 0.94)	0.034
ACEI (14-day gap)	50,470	****	****	****	****	1.3	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 48. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Neverland	Person	Average Person	Average Person	Newskan	Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio (95% Confidence	Wald
	Number of		Days at			per 1,000 Person		1,000 Person	1,000	•	
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Unknown											
Site-Adjusted Analysis		****	****	****	****		****				
SV (14-day gap, history of	11,656	****	****	****	****	0.25	****	4.60	****	0.40./.0.000.00\	0.044
ACEI (-183, -1))								-1.68	***	0.13 (0.02, 0.92)	0.041
ACEI (14-day gap)	99,645	****	****	****	****	1.93	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05						
SV (14-day gap, history of	11,647	****	****	****	****	0.45	****				
ACEI (-183, -1))								-0.45	****	0.50 (0.05, 5.51)	0.571
ACEI (14-day gap)	11,647	****	****	****	****	0.91	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	11,647	****	****	****	****	0.25	****				
ACEI (-183, -1))								-1.06	****	0.20 (0.02, 1.63)	0.132
ACEI (14-day gap)	11,647	****	****	****	****	1.31	****				
Race: American Indian	,										
Site-Adjusted Analysis											
SV (14-day gap, history of	242	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	4,525	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	234	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	234	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	234	****	****	****	****	0	****				
ACEI (-1831))								0	****	-	-
ACEI (14-day gap)	234	****	****	****	****	0	****				

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Table 48. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person	Average Person	Average Person	Normala	Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Years at Risk	Days at Risk	Years at Risk	of Events	per 1,000 Person		1,000 Person	1,000 New Users	Interval) ²	P-Value ²
Race: Asian	New Users	RISK	RISK	RISK	or Events	Years	Users	Years	New Osers	intervaij	P-value
Site-Adjusted Analysis		****	****	****	****	^	****				
SV (14-day gap, history of	666	4.4.4.4.4	4.4.4.4.4	4. 4. 4. 4. 4.	4.4.4.4.4	0	4-4-4-4-4-	0.00	****		
ACEI (-183, -1))	7.074	****	****	****	****	0.00	****	-0.99		-	-
ACEI (14-day gap)	7,871					0.99	****				
Fixed Ratio 1:1 Propensity So	ore Matched										
SV (14-day gap, history of	656	****	****	****	****	0	****				
ACEI (-183, -1))								-8.2	****	-	-
ACEI (14-day gap)	656	****	****	****	****	8.2	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	656	****	****	****	****	0	****				_
ACEI (-183, -1))								-3.98	****	-	-
ACEI (14-day gap)	656	****	****	****	****	3.98	****				
Race: Black											
Site-Adjusted Analysis											
SV (14-day gap, history of	9,015	****	****	****	****	2.61	****				
ACEI (-1831))	•							-4.74	****	0.34 (0.16, 0.73)	0.005
ACEI (14-day gap)	92,098	****	****	****	****	7.35	****				
Fixed Ratio 1:1 Propensity So		Condition	al Analysi	s: Caliper=	: 0.05 ¹						
SV (14-day gap, history of	8.997	****	****	****	****	3.33	****				
ACEI (-1831))	0,557					5.55		-3.33	****	0.50 (0.17, 1.46)	0.206
ACEI (-183, -1)) ACEI (14-day gap)	8,997	****	****	****	****	6.67	****	5.55		0.50 (0.17) 1.10)	0.200
Fixed Ratio 1:1 Propensity So		Unconditi	ional Anal	vsis: Calina	er= 0 05	0.07					
SV (14-day gap, history of	8,997	****	****	****	*****	2.62	****				
, , , , , ,	0,337					2.02		-2.4	****	0.50 (0.20, 1.21)	0.125
ACEI (-183, -1))	0.007	****	****	****	****	F 02	****	-2.4		0.30 (0.20, 1.21)	0.123
ACEI (14-day gap)	8,997	ጥጥጥጥ	ጥጥጥጥ	ጥጥጥጥ	ጥጥጥጥ	5.02	ጥጥጥጥ				

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Table 48. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Person	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Pacific Islander											
Site-Adjusted Analysis											
SV (14-day gap, history of	66	****	****	****	****	0	****				
ACEI (-183, -1))								-3.59	****	-	-
ACEI (14-day gap)	741	****	****	****	****	3.59	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	59	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	59	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	59	****	****	****	****	0	****				
ACEI (-183, -1))								0	****	-	-
ACEI (14-day gap)	59	****	****	****	****	0	****				
Race: White											
Site-Adjusted Analysis											
SV (14-day gap, history of	47,994	****	****	****	****	0.75	****				
ACEI (-183, -1))								-0.46	****	0.60 (0.34, 1.04)	0.069
ACEI (14-day gap)	490,002	****	****	****	****	1.21	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	47,950	****	****	****	****	0.79	****				
ACEI (-183, -1))								-1.19	****	0.40 (0.18, 0.91)	0.028
ACEI (14-day gap)	47,950	****	****	****	****	1.99	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	onal Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	47,950	****	****	****	****	0.75	****				_
ACEI (-183, -1))								-0.51	****	0.56 (0.29, 1.10)	0.091
ACEI (14-day gap)	47,950	****	****	****	****	1.26	****				

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 49. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval)	Wald P-Value
Site-Adjusted Analysis											
SV (14-day gap, history of	49,140	****	****	****	****	0.53	****				
ARBs (-183, -1))								-0.36	****	0.57 (0.29, 1.12)	0.101
ARBs (14-day gap)	337,083	****	****	****	****	0.9	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	: 0.05 ¹						
SV (14-day gap, history of	49,137	****	****	****	****	0.78	****				
ARBs (-183, -1))								-0.19	****	0.80 (0.32, 2.03)	0.638
ARBs (14-day gap)	49,137	****	****	****	****	0.97	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipo	er= 0.05						
SV (14-day gap, history of	49,137	****	****	****	****	0.53	****				
ARBs (-183, -1))								-0.33	****	0.59 (0.27, 1.31)	0.193
ARBs (14-day gap)	49,137	****	****	****	****	0.86	****				

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 50. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)

		Person	Average Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at	Number	per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
No Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	49,082	****	****	****	****	0.53	****				
ARBs (-183, -1))								-0.24	****	0.66 (0.34, 1.31)	0.234
ARBs (14-day gap)	336,258	****	****	****	****	0.78	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	0.051						
SV (14-day gap, history of	49,079	****	****	****	****	0.78	****				
ARBs (-183, -1))								0	****	1.00 (0.38, 2.66)	1
ARBs (14-day gap)	49,079	****	****	****	****	0.78	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Uncondit	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	49,079	****	****	****	****	0.53	****				_
ARBs (-183, -1))								-0.24	****	0.67 (0.30, 1.50)	0.329
ARBs (14-day gap)	49,079	****	****	****	****	0.77	****				
Angioedema (-183, -1)											
Site-Adjusted Analysis											
SV (14-day gap, history of	58	****	****	****	****	0	****				
ARBs (-183, -1))								-52.37	****	-	-
ARBs (14-day gap)	825	****	****	****	****	52.37	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	55	****	****	****	****	0	****				
ARBs (-183, -1))								-186.22	****	-	-
ARBs (14-day gap)	55	****	****	****	****	186.22	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Uncondit	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	55	****	****	****	****	0	****				
ARBs (-183, -1))								-74.99	****	-	-
ARBs (14-day gap)	55	****	****	****	****	74.99	****				

 $^{^{1}\}mbox{Conditional}$ analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 51. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)

Medical Product New Users Risk Risk Risk Risk Fevents Vears Vears Vears New Users Interval] P-Value		Number of	Person Years at	Person	Average Person	Number	Incidence Rate	Risk per 1,000 New	Incidence Rate Difference per 1.000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
No Angioedema (ever, -1) Site-Adjusted Analysis SV (14-day gap, history of A8,390 ******	Modical Product			•			• •	_	,	•	•	
Site-Adjusted Analysis SV (14-day gap, history of 48,390 ******		New Osers	RISK	RISK	RISK	or Events	rears	Users	rears	New Osers	intervaij	P-value
SV (14-day gap, history of A8,390 ******	_ , , ,											
ARBs (1-83, -1)) ARBs (1-4 dy gap) 329,726 ***** **** ***** ***** 0.68 ***** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ SV (14-day gap, history of 48,383 **** **** **** ***** 0.79 ***** ARBs (1-83, -1)) ARBs (1-83, -1) ARBs (1-83,		49 200	****	****	****	****	0.54	****				
ARBS (14-day gap) 329,726 ***** **** **** ***** 0.68 ***** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ SV (14-day gap, history of 48,383 **** **** **** **** 0.79 ***** ARBS (183, -1)) ARBS (14-day gap) 48,383 **** **** **** **** 0.59 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 48,383 **** **** **** **** 0.54 ***** ARBS (183, -1)) ARBS (183, -1) ARBS (14-day gap) 48,383 **** **** **** **** 0.69 ***** Angioedema (ever, -1) Site-Adjusted Analysis SV (14-day gap, history of 750 **** **** **** **** 0.69 ***** ARBS (1-4ay gap) 7,357 **** **** **** **** 0		46,330					0.54		-0.14	****	077/039 153)	0.459
Series S	. ,	220 726	****	****	****	****	0.60	****	-0.14		0.77 (0.33, 1.33)	0.433
SV (14-day gap, history of A8,383				1 4 1 1	6 !!		0.08					
ARBs (-183, -1)) ARBs (14-day gap) 48,383 **** **** **** **** **** **** ****							0.70	****				
ARBs (14-day gap) 48,383 **** **** **** ***** 0.59 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 48,383 **** **** **** **** 0.54 ***** ARBs (14-day gap) 48,383 **** **** **** **** 0.54 ***** ARBs (14-day gap) 48,383 **** **** **** **** 0.69 ***** ARBs (14-day gap) 48,383 **** **** **** **** 0.69 ***** Site-Adjusted Analysis SV (14-day gap, history of 750 **** **** **** **** 0 ***** ARBs (14-day gap) 7,357 **** **** **** **** 10.71 ***** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** 0 ***** ARBs (-183, -1))	, , , , , ,	48,383	****	****	****	****	0.79	****	0.3	****	1 22 / 0 46 2 04)	0.504
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper = 0.05 SV (14-day gap, history of 48,383 **** **** ***** ***** ***** 0.54 ***** ARBS (-183, -1)) ARBS (14-day gap) 48,383 **** **** ***** ***** ***** 0.69 ***** Angioedema (ever, -1) Site-Adjusted Analysis SV (14-day gap, history of 750 **** **** ***** ***** ***** 0 ****** ARBS (-183, -1)) ARBS (14-day gap) 7,357 ***** **** ***** ***** ***** 10.71 ****** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper = 0.05 SV (14-day gap, history of 744 ***** ***** ***** ***** 0 ***** ARBS (-183, -1)) ARBS (-183, -1)) Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper = 0.05 SV (14-day gap, history of 744 ***** ***** ***** ***** 0 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper = 0.05 SV (14-day gap, history of 744 ***** ***** ***** ***** 0 ****** ARBS (1-183, -1)) SV (14-day gap, history of 744 ***** ***** ***** ***** 0 ****** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper = 0.05 SV (14-day gap, history of 744 ***** ***** ***** ***** 0 ****** ARBS (-183, -1))	` ' ''		ale ale ale ale ale		ale ale ale ale	0.2	4. 4. 4. 4.	1.33 (0.46, 3.84)	0.594			
SV (14-day gap, history of 48,383 **** **** **** ***** ***** 0.54 ***** ARBs (-183, -1)) ARBs (14-day gap) 48,383 **** **** **** **** **** 0.69 ***** Angioedema (ever, -1) Site-Adjusted Analysis SV (14-day gap, history of 750 **** **** **** ***** 0 ***** ARBs (-183, -1)) ARBs (14-day gap) 7,357 **** **** **** **** **** **** 10.71 ***** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** **** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** **** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** **** 0 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** 0 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** **** 0 ***** ARBs (-183, -1))				*****			0.59	****				
ARBs (-183, -1)) ARBs (14-day gap)								de de de de de				
ARBs (14-day gap) 48,383 ***** **** ***** ***** 0.69 ***** Angioedema (ever, -1) Site-Adjusted Analysis SV (14-day gap, history of 750 ***** **** **** ***** 10.71 *****		48,383	****	****	****	****	0.54	****				
Angioedema (ever, -1) Site-Adjusted Analysis SV (14-day gap, history of 750 ***** ***** ***** ***** 0 ****** ARBs (-183, -1)) Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 SV (14-day gap) 744 ***** ***** ***** ***** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 ***** ***** ***** ***** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 ***** ***** ***** ***** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 ***** ***** ***** 0 ****** ARBs (-183, -1)) -8.72 *****									-0.15	****	0.76 (0.33, 1.74)	0.515
Site-Adjusted Analysis SV (14-day gap, history of 750 ***** ***** ***** ***** ***** ***** 0 ******		48,383	****	****	****	****	0.69	****				
SV (14-day gap, history of 750 **** **** **** **** **** 0 ***** ARBs (-183, -1)) ARBs (14-day gap) 7,357 **** **** **** **** 10.71 ***** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** 0 ***** ARBs (-183, -1)) ARBs (14-day gap) 744 **** **** **** **** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** 0 ***** ARBs (-183, -1)) -8.72 *****												
ARBs (-183, -1)) Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ SV (14-day gap) 7,44 ***** **** **** ***** ***** ***** * 10.71 ****** ARBs (-183, -1)) ARBs (14-day gap) 744 ***** **** **** ***** **** **** * 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05¹ SV (14-day gap, history of 744 ***** **** ***** ***** ***** * 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 ***** ***** ***** ***** * 0 ****** ARBs (-183, -1)) ARBs (-183, -1))												
ARBs (14-day gap) 7,357 **** **** **** **** 10.71 ***** Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** 10.71 ***** ARBs (1-83, -1)) ARBs (14-day gap) 744 **** **** **** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** 0 *****	SV (14-day gap, history of	750	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 ***** ***** ***** 0 ******	ARBs (-183, -1))								-10.71	****	-	-
SV (14-day gap, history of 744 **** **** **** **** 0 ***** - 19.05 ***** 19.05 *****	ARBs (14-day gap)	7,357	****	****	****	****	10.71	****				
SV (14-day gap, history of 744 **** **** **** **** 0 ***** - 19.05 ***** 19.05 *****	Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	0.051						
ARBs (-183, -1)) ARBs (14-day gap) 744 **** **** **** **** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** **** 0 ***** ARBs (-183, -1)) -8.72 *****							0	****				
ARBs (14-day gap) 744 **** **** **** 19.05 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 SV (14-day gap, history of 744 **** **** **** 0 ***** ARBs (-183, -1)) -8.72 ****									-19.05	****	-	-
SV (14-day gap, history of 744 **** **** ***** 0 ***** ARBs (-183, -1)) -8.72 ****		744	****	****	****	****	19.05	****				
ARBs (-183, -1)) -8.72 *****		core Matched	Uncondit	ional Anal	ysis; Calipe	er= 0.05						
ARBs (-183, -1)) -8.72 *****	SV (14-day gap, history of	744	****	****	****	****	0	****				
									-8.72	****	-	-
AUD2 (14-na) Rah) 144 0.1/2	ARBs (14-day gap)	744	****	****	****	****	8.72	****				

 $^{^{1}\}mbox{Conditional}$ analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

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Table 52. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies

	Number of	Person Years at	Person	Average Person Years at	Numbor	Incidence Rate	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Days at Risk	Risk	of Events	• '	Users	Years	New Users	Interval)	P-Value
No Serious allergies	New Osers	NISK	NISK	NISK	OI EVEIILS	Tears	USEIS	Tears	New Osers	iiitei vaij	r-value
Site-Adjusted Analysis											
SV (14-day gap, history of	42,674	****	****	****	****	0.54	****				
ARBs (-183, -1))	42,074					0.54		-0.15	****	0.74 (0.36, 1.53)	0.418
ARBs (14-day gap)	282,648	****	****	****	****	0.69	****	0.13		0.74 (0.50, 1.55)	0.410
Fixed Ratio 1:1 Propensity Sc		Condition	al Analysi	s. Calinar-	0.0E ¹	0.03					
	42.666	****	*****	*****	*****	0.77	****				
SV (14-day gap, history of	42,000					0.77		0.11	****	1.17 (0.39, 3.47)	0.782
ARBs (-183, -1))	42,666	****	****	****	****	0.66	****	0.11		1.17 (0.33, 3.47)	0.762
ARBs (14-day gap) Fixed Ratio 1:1 Propensity So						0.00					
SV (14-day gap, history of	42.666	****	****	****	****	0.54	****				
	42,000					0.54		-0.09	****	0.84 (0.34, 2.05)	0.7
ARBs (-183, -1))	42,666	****	****	****	****	0.62	****	-0.03		0.84 (0.34, 2.03)	0.7
ARBs (14-day gap) Serious allergies	42,000					0.02					
Site-Adjusted Analysis											
SV (14-day gap, history of	6.466	****	****	****	****	0.5	****				
ARBs (-183, -1))	0,400					0.5		-1.61	****	0.23 (0.03, 1.68)	0.147
ARBs (14-day gap)	54,435	****	****	****	****	2.11	****			0.20 (0.00) 2.00)	0.2.7
Fixed Ratio 1:1 Propensity Sc		Condition	al Analysi	s· Caliner=	0.051	2.11					
SV (14-day gap, history of	6.436	****	****	*****	****	0.84	****				
ARBs (-183, -1))	0,430					0.04		-1.69	****	0.33 (0.03, 3.20)	0.341
ARBs (14-day gap)	6,436	****	****	****	****	2.53	****	2.03		0.55 (0.05) 5.20)	0.011
Fixed Ratio 1:1 Propensity So		Unconditi	ional Anal	vsis: Caline	er= 0.05	2.33					
SV (14-day gap, history of	6,436	****	****	****	****	0.5	****				
ARBs (-183, -1))	0,450					0.5		-1.42	****	0.25 (0.03, 2.11)	0.201
ARBs (14-day gap)	6,436	****	****	****	****	1.92	****			(,)	
· · · · - · · · · · · · · · · · · · · ·	٥, . ٠ ٠										

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 53. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Sex

		Person	Average Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	
	Number of	Years at	Days at	Years at		per 1,000 Person	New	1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval)	P-Value
Sex: Male											
Site-Adjusted Analysis	22.24	****	****	****	****	0.00	****				
SV (14-day gap, history of	29,914	****	****	****	****	0.29	****	0.64	****	0.24 (0.40	0.045
ARBs (-183, -1))		de de de de de		4.4.4.4.4				-0.61	***	0.31 (0.10, 0.98)	0.045
ARBs (14-day gap)	149,212	****	****	****	****	0.9	****				
Fixed Ratio 1:1 Propensity So	ore Matched				0.05						
SV (14-day gap, history of	29,883	****	****	****	****	0.48	****				
ARBs (-183, -1))								-0.32	****	0.60 (0.14, 2.51)	0.484
ARBs (14-day gap)	29,883	****	****	****	****	0.8	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	29,883	****	****	****	****	0.29	****				
ARBs (-183, -1))								-0.55	****	0.33 (0.09, 1.20)	0.092
ARBs (14-day gap)	29,883	****	****	****	****	0.83	****				
Sex: Female											
Site-Adjusted Analysis											
SV (14-day gap, history of	19,226	****	****	****	****	0.93	****				
ARBs (-183, -1))								0.03	****	0.98 (0.43, 2.26)	0.971
ARBs (14-day gap)	187,871	****	****	****	****	0.89	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	19,218	****	****	****	****	1.51	****				
ARBs (-1831))	•							0.5	****	1.50 (0.42, 5.32)	0.53
ARBs (14-day gap)	19,218	****	****	****	****	1	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	19,218	****	****	****	****	0.93	****				
ARBs (-1831))	•							0.35	****	1.53 (0.47, 5.03)	0.482
ARBs (14-day gap)	19,218	****	****	****	****	0.58	****			•	

¹Conditional analysis accounts for informative events and person-time.

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^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



Table 54. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Age Group: 18-44 Years										·	
Site-Adjusted Analysis											
SV (14-day gap, history of	1,164	****	****	****	****	0	****				_
ARBs (-183, -1))								-2.74	****	-	-
ARBs (14-day gap)	8,502	****	****	****	****	2.74	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	1,154	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	1,154	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05											
SV (14-day gap, history of	1,154	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	1,154	****	****	****	****	0	****				
Age Group: 45-54 Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	2,653	****	****	****	****	0	****				
ARBs (-183, -1))								-2.01	****	-	-
ARBs (14-day gap)	18,293	****	****	****	****	2.01	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	0.051						
SV (14-day gap, history of	2,641	****	****	****	****	0	****				
ARBs (-183, -1))								-4.24	****	-	-
ARBs (14-day gap)	2,641	****	****	****	****	4.24	****				
Fixed Ratio 1:1 Propensity So	core Matched			ysis; Calipe	er= 0.05						
SV (14-day gap, history of	2,641	****	****	****	****	0	****				
ARBs (-183, -1))								-2.03	****	-	-
ARBs (14-day gap)	2,641	****	****	****	****	2.03	****				

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Table 54. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group

	Number of	Person Years at	Person	Average Person	Number	Incidence Rate	Risk per 1,000 New	Incidence Rate Difference per 1.000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	• •	Users	Years	New Users	Interval) ²	P-Value ²
Age Group: 55-64 Years	New Osers	NISK	NISK	NISK	OI EVEIRS	Tears	USEIS	Tears	New Osers	ilitei vaij	r-value
Site-Adjusted Analysis											
SV (14-day gap, history of	5,990	****	****	****	****	1.03	****				
ARBs (-183, -1))	3,990					1.03		-0.88	****	0.58 (0.14, 2.44)	0.461
ARBS (-183, -1)) ARBS (14-day gap)	40.547	****	****	****	****	1.91	****	-0.00		0.38 (0.14, 2.44)	0.401
		Candition	al Analusi	a. Calinan	0.051	1.71					
Fixed Ratio 1:1 Propensity So		****	****	*****	****	4.70	****				
SV (14-day gap, history of	5,945	****	****	****	****	1.79	****	0	****	1.00/014 7.10	4
ARBs (-183, -1))			4.4.4.4.					0	4. 4. 4. 4.	1.00 (0.14, 7.10)	1
ARBs (14-day gap)	5,945	****	****	****	****	1.79	****				
Fixed Ratio 1:1 Propensity So											
SV (14-day gap, history of	5,945	****	****	****	****	1.03	****				
ARBs (-183, -1))								0.19	****	1.17 (0.16, 8.33)	0.876
ARBs (14-day gap)	5,945	****	****	****	****	0.85	****				
Age Group: 65+ Years											
Site-Adjusted Analysis											
SV (14-day gap, history of	39,333	****	****	****	****	0.51	****				
ARBs (-183, -1))								-0.15	****	0.72 (0.33, 1.55)	0.399
ARBs (14-day gap)	269,741	****	****	****	****	0.66	****				
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ¹											
SV (14-day gap, history of	39.269	****	****	****	****	0.7	****				
ARBs (-183, -1))	,							-0.23	****	0.75 (0.26, 2.16)	0.594
ARBs (14-day gap)	39,269	****	****	****	****	0.94	****			, , ,	
Fixed Ratio 1:1 Propensity So		Uncondit	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	39,269	****	****	****	****	0.51	****				
ARBs (-183, -1))	,							-0.26	****	0.63 (0.25, 1.55)	0.311
ARBs (14-day gap)	39,269	****	****	****	****	0.77	****			(,)	
1 day 8ap	33,203					0.77					

¹Conditional analysis accounts for informative events and person-time.

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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

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Table 55. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate per 1,000 Person	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Unknown											
Site-Adjusted Analysis											
SV (14-day gap, history of	8,082	****	****	****	****	0	****				
ARBs (-183, -1))								-0.63	****	-	-
ARBs (14-day gap)	47,793	****	****	****	****	0.63	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysi	s; Caliper=	0.05						
SV (14-day gap, history of	8,026	****	****	****	****	0	****				
ARBs (-183, -1))								-1.28	****	-	-
ARBs (14-day gap)	8,026	****	****	****	****	1.28	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	8,026	****	****	****	****	0	****				
ARBs (-183, -1))								-0.59	****	-	-
ARBs (14-day gap)	8,026	****	****	****	****	0.59	****				
Race: American Indian											
Site-Adjusted Analysis											
SV (14-day gap, history of	133	****	****	****	****	0	****				
ARBs (-183, -1))								-1.36	****	-	-
ARBs (14-day gap)	1,948	****	****	****	****	1.36	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	131	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	131	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	131	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	131	****	****	****	****	0	****				

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Table 55. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

	Number of	Person Years at	Average Person Days at	Average Person Years at	Number	Incidence Rate	Risk per 1,000 New	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	• '	Users	Years	New Users	· Interval) ²	P-Value ²
Race: Asian		11.01.	11.011		01 21 0110				11011 00010		1 10.00
Site-Adjusted Analysis											
SV (14-day gap, history of	1,070	****	****	****	****	0	****				
ARBs (-183, -1))	•							-0.54	****	-	-
ARBs (14-day gap)	7,811	****	****	****	****	0.54	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	1,026	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	1,026	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	1,026	****	****	****	****	0	****				
ARBs (-183, -1))								-2.15	****	-	-
ARBs (14-day gap)	1,026	****	****	****	****	2.15	****				
Race: Black											
Site-Adjusted Analysis											
SV (14-day gap, history of	6,989	****	****	****	****	0.97	****				
ARBs (-183, -1))								-1.82	****	0.33 (0.08, 1.35)	0.122
ARBs (14-day gap)	55,801	****	****	****	****	2.79	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Condition	al Analysis	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	6,967	****	****	****	****	0.82	****				
ARBs (-183, -1))								-2.46	****	0.25 (0.03, 2.24)	0.215
ARBs (14-day gap)	6,967	****	****	****	****	3.28	****				
Fixed Ratio 1:1 Propensity Sc	ore Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	6,967	****	****	****	****	0.97	****				
ARBs (-183, -1))								-1.24	****	0.39 (0.08, 1.95)	0.253
ARBs (14-day gap)	6,967	****	****	****	****	2.21	****				

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Table 55. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race

		Person	Person	Average Person		Incidence Rate	Risk per 1,000	Incidence Rate Difference per	Difference in Risk per	Hazard Ratio	187 -14
	Number of	Years at	Days at	Years at		per 1,000 Person		1,000 Person	1,000	(95% Confidence	Wald
Medical Product	New Users	Risk	Risk	Risk	of Events	Years	Users	Years	New Users	Interval) ²	P-Value ²
Race: Pacific Islander											
Site-Adjusted Analysis											
SV (14-day gap, history of	61	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	478	****	****	****	****	0	****				_
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysis	s; Caliper=	0.05						
SV (14-day gap, history of	50	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	50	****	****	****	****	0	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	50	****	****	****	****	0	****				
ARBs (-183, -1))								0	****	-	-
ARBs (14-day gap)	50	****	****	****	****	0	****				
Race: White											
Site-Adjusted Analysis											
SV (14-day gap, history of	32,805	****	****	****	****	0.6	****				
ARBs (-183, -1))								0.03	****	1.00 (0.46, 2.19)	0.996
ARBs (14-day gap)	223,252	****	****	****	****	0.57	****				
Fixed Ratio 1:1 Propensity So	core Matched	Condition	al Analysi	s; Caliper=	0.05 ¹						
SV (14-day gap, history of	32,796	****	****	****	****	0.83	****				
ARBs (-183, -1))								-0.14	****	0.86 (0.29, 2.55)	0.782
ARBs (14-day gap)	32,796	****	****	****	****	0.97	****				
Fixed Ratio 1:1 Propensity So	core Matched	Unconditi	ional Anal	ysis; Calipe	er= 0.05						
SV (14-day gap, history of	32,796	****	****	****	****	0.6	****				
ARBs (-183, -1))								0.07	****	1.10 (0.40, 3.04)	0.854
ARBs (14-day gap)	32,796	****	****	****	****	0.53	****				

¹Conditional analysis accounts for informative events and person-time.

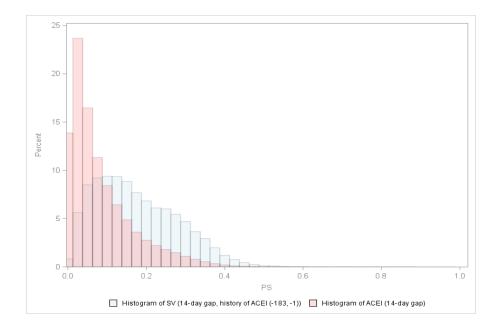
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²Data presented by a dash are unable to be calculated. This table may not use all data representations.

^{*****}Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.



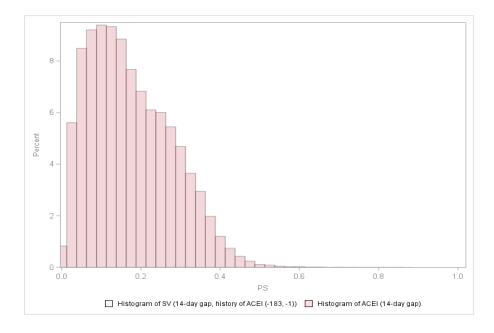
Figure 1a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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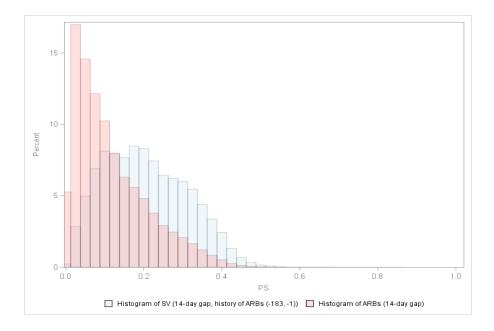
Figure 1b. Histogram of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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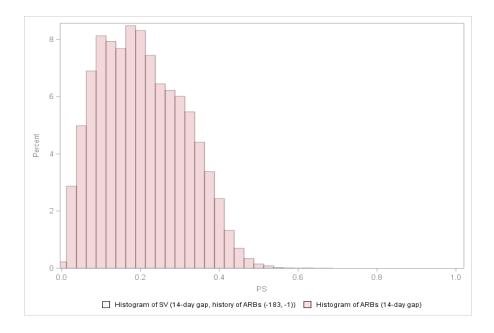
Figure 2a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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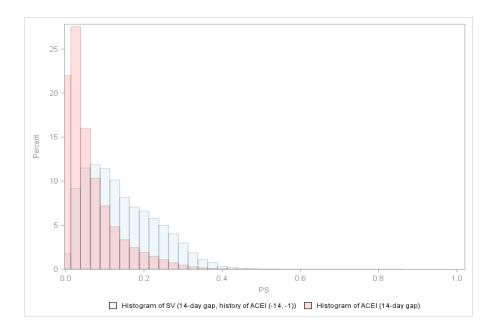
Figure 2b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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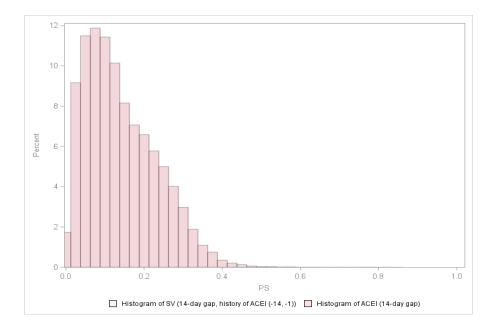
Figure 3a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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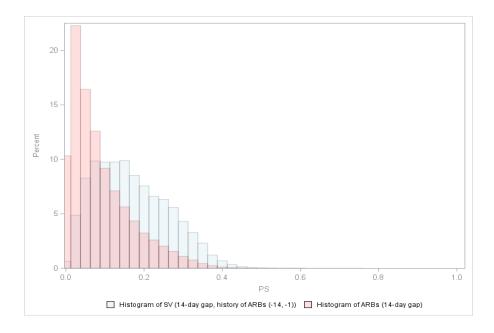
Figure 3b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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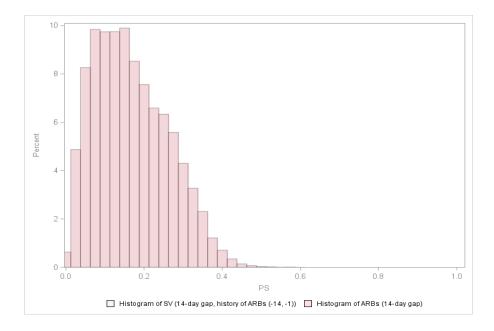
Figure 4a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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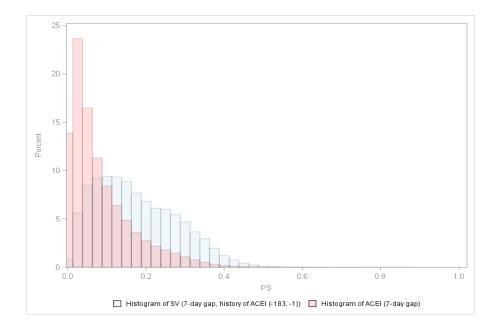
Figure 4b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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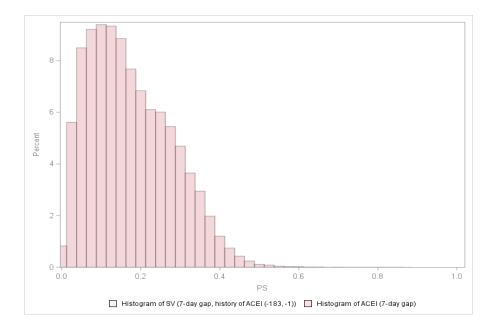
Figure 5a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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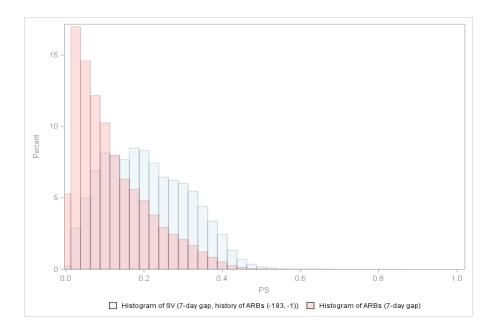
Figure 5b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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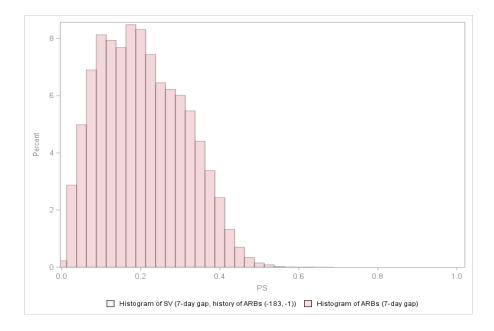
Figure 6a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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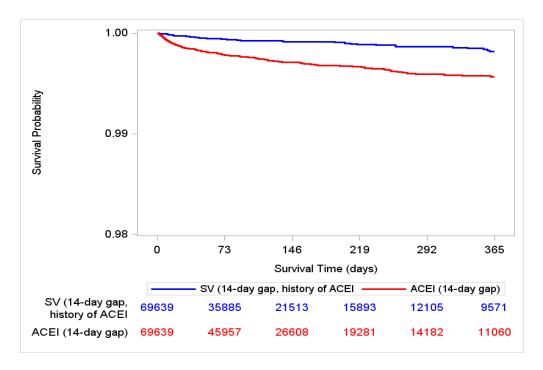
Figure 6b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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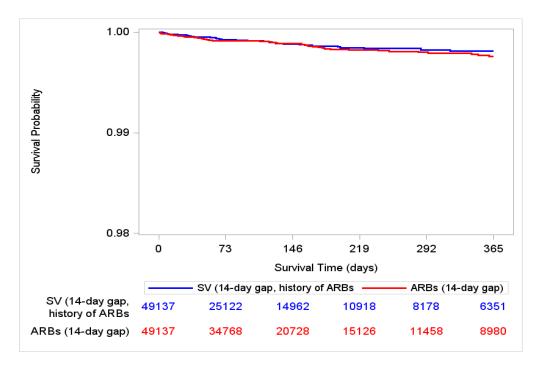
Figure 7. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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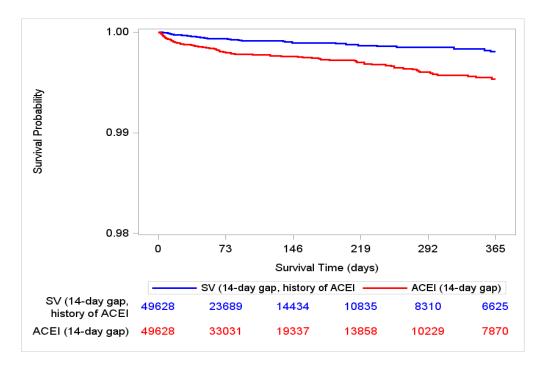
Figure 8. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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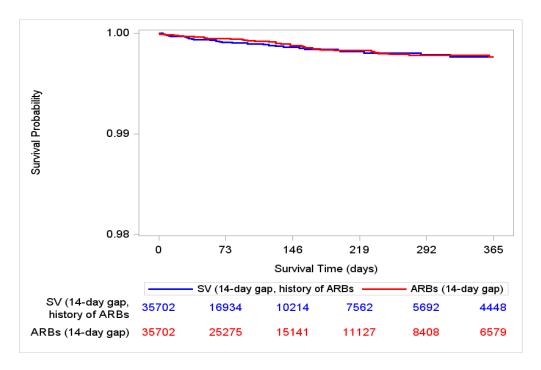
Figure 9. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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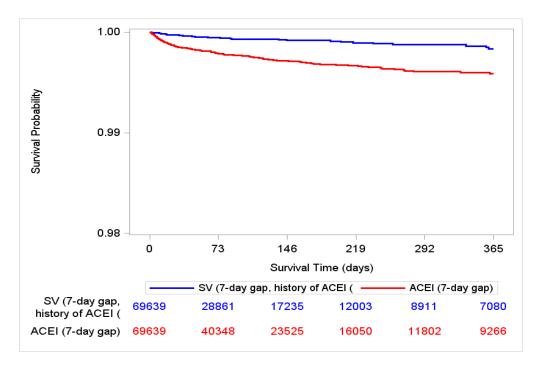
Figure 10. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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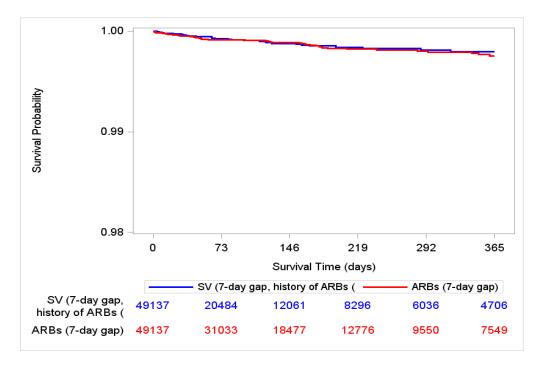
Figure 11. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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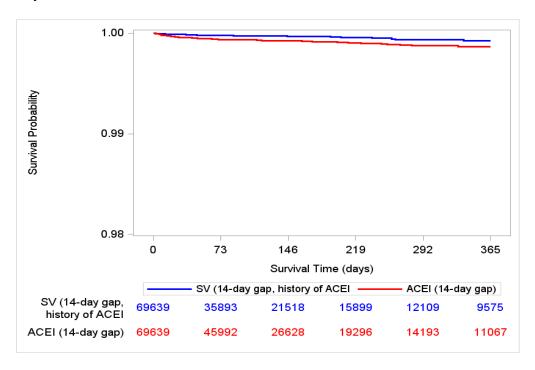
Figure 12. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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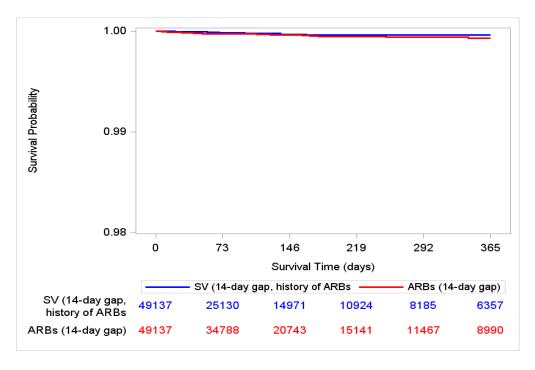
Figure 13. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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Figure 14. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020

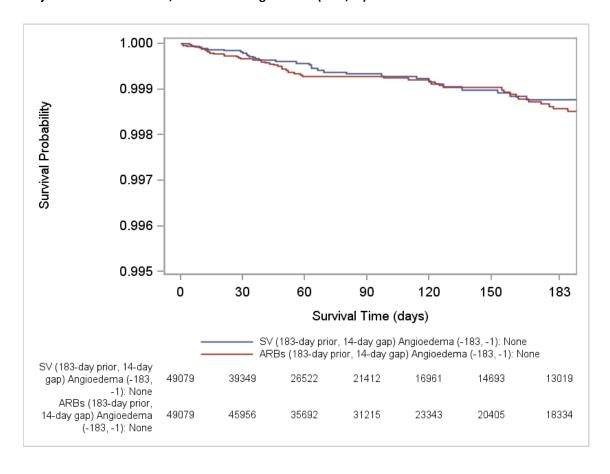


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Figure 15. Kaplan Meier Survival Curves for Risk of Angioedema, SV (183 days prior, 14-day gap) and ARBs (183 days prior, 14-day gap)

Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort, No Baseline Angioedema (-183, -1)

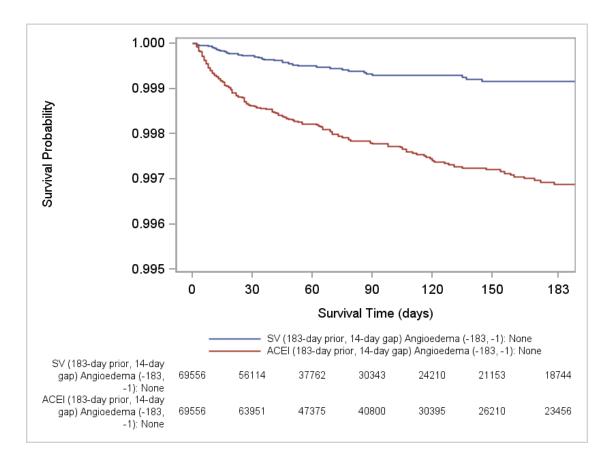


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Figure 16. Kaplan Meier Survival Curves for Risk of Angioedema, SV (183 days prior, 14-day gap) and ACEI (183 days prior, 14-day gap)

Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort, Angioedema, No Baseline Angioedema (-183, -1)



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Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (January 13, 2021)

DP ID	Start Date ¹	End Date ¹
DP01	1/1/2010	12/31/2019
DP02	1/1/2008	12/31/2019
DP03	1/1/2008	2/29/2020
DP04	6/1/2007	10/31/2019
DP05	1/1/2006	1/31/2020

¹The start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

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Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name Brand Name

Angiotensin-Converting Enzyme Inhibitors (ACEI)

AMLODIPINE BESYLATE/BENAZEPRIL HCL Lotrel

AMLODIPINE BESYLATE/BENAZEPRIL HCL amlodipine-benazepril

BENAZEPRIL HCL

BENAZEPRIL HCL

BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE

Lotensin HCT

BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE benazepril-hydrochlorothiazide

CAPTOPRIL captopril

CAPTOPRIL/HYDROCHLOROTHIAZIDE captopril-hydrochlorothiazide

ENALAPRIL MALEATE Epaned ENALAPRIL MALEATE Vasotec

ENALAPRIL MALEATE enalapril maleate

ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE Vaseretic

ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE enalapril-hydrochlorothiazide

FOSINOPRIL SODIUM fosinopril

FOSINOPRIL SODIUM/HYDROCHLOROTHIAZIDE fosinopril-hydrochlorothiazide

LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL/HYDROCHLOROTHIAZIDE

Prinivil
Qbrelis
Zestril
LISINOPRIL
LISINOPRIL
Zestoretic

LISINOPRIL/HYDROCHLOROTHIAZIDE lisinopril-hydrochlorothiazide

MOEXIPRIL HCL Univasc
MOEXIPRIL HCL moexipril
MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE Uniretic

MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE moexipril-hydrochlorothiazide

PERINDOPRIL ARGININE/AMLODIPINE BESYLATE Prestalia
PERINDOPRIL ERBUMINE Aceon

PERINDOPRIL ERBUMINE perindopril erbumine

QUINAPRIL HCL Accupril
QUINAPRIL HCL quinapril
QUINAPRIL HCL/HYDROCHLOROTHIAZIDE Accuretic

QUINAPRIL HCL/HYDROCHLOROTHIAZIDE quinapril-hydrochlorothiazide

RAMIPRIL Altace
RAMIPRIL ramipril
TRANDOLAPRIL Mavik
TRANDOLAPRIL trandolapril
TRANDOLAPRIL/VERAPAMIL HCL Tarka

TRANDOLAPRIL/VERAPAMIL HCL trandolapril-verapamil amlodipine besylate/benazepril HCl amlodipine-benazepril

benazepril HCl Lotensin
benazepril HCl benazepril
captopril captopril

enalapril maleate enalapril maleate

lisinopril lisinopril

lisinopril/hydrochlorothiazide lisinopril-hydrochlorothiazide

quinapril HClquinaprilramiprilramipriltrandolapriltrandolapril

Angiotensin II Receptor Blockers (ARB)



Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name

AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL

AMLODIPINE BESYLATE/VALSARTAN AMLODIPINE BESYLATE/VALSARTAN

AMLODIPINE BESYLATE/VALSARTAN /HYDROCHLOROTHIAZIDE AMLODIPINE BESYLATE/VALSARTAN /HYDROCHLOROTHIAZIDE

AZILSARTAN MEDOXOMIL

AZILSARTAN MEDOXOMIL/CHLORTHALIDONE

CANDESARTAN CILEXETIL CANDESARTAN CILEXETIL

CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE

EPROSARTAN MESYLATE EPROSARTAN MESYLATE

EPROSARTAN MESYLATE/HYDROCHLOROTHIAZIDE

IRBESARTAN IRBESARTAN

IRBESARTAN/HYDROCHLOROTHIAZIDE IRBESARTAN/HYDROCHLOROTHIAZIDE

LOSARTAN POTASSIUM LOSARTAN POTASSIUM

LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE

LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE

NEBIVOLOL HCL/VALSARTAN OLMESARTAN MEDOXOMIL OLMESARTAN MEDOXOMIL

OLMESARTAN MEDOXOMIL/AMLODIPINE

BESYLATE/HYDROCHLOROTHIAZIDE

OLMESARTAN MEDOXOMIL/AMLODIPINE

BESYLATE/HYDROCHLOROTHIAZIDE

OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE

TELMISARTAN TELMISARTAN

TELMISARTAN/AMLODIPINE BESYLATE

TELMISARTAN/AMLODIPINE BESYLATE TELMISARTAN/HYDROCHLOROTHIAZIDE

TELMISARTAN/HYDROCHLOROTHIAZIDE

VALSARTAN VALSARTAN

VALSARTAN/HYDROCHLOROTHIAZIDE VALSARTAN/HYDROCHLOROTHIAZIDE

amlodipine besylate/olmesartan medoxomil

amlodipine besylate/valsartan

amlodipine besylate/valsartan/hydrochlorothiazide

candesartan cilexetil

candesartan cilexetil/hydrochlorothiazide candesartan cilexetil/hydrochlorothiazide

irbesartan

irbesartan/hydrochlorothiazide

Brand Name

Azor

amlodipine-olmesartan

Exforge

amlodipine-valsartan

Exforge HCT

amlodipine-valsartan-hcthiazid

Edarbi Edarbyclor Atacand candesartan Atacand HCT

candesartan-hydrochlorothiazid

Teveten eprosartan Teveten HCT Avapro irbesartan Avalide

irbesartan-hydrochlorothiazide

Cozaar Iosartan Hyzaar

losartan-hydrochlorothiazide

Byvalson Benicar olmesartan Tribenzor

olmesartan-amlodipin-hcthiazid

Benicar HCT

olmesartan-hydrochlorothiazide

Micardis telmisartan Twynsta

telmisartan-amlodipine

Micardis HCT

telmisartan-hydrochlorothiazid

Diovan valsartan Diovan HCT

valsartan-hydrochlorothiazide amlodipine-olmesartan amlodipine-valsartan

amlodipine-valsartan-hcthiazid

Atacand candesartan Atacand HCT

candesartan-hydrochlorothiazid

irbesartan

irbesartan-hydrochlorothiazide

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Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name Brand Name

losartan potassium losartan

losartan potassium/hydrochlorothiazide losartan-hydrochlorothiazide

olmesartan medoxomil Benicar olmesartan medoxomil olmesartan

olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide olmesartan-amlodipin-hcthiazid

olmesartan medoxomil/hydrochlorothiazide Benicar HCT telmisartan telmisartan

telmisartan/hydrochlorothiazide telmisartan-hydrochlorothiazid

valsartan valsartan

valsartan/hydrochlorothiazide valsartan-hydrochlorothiazide

Sacubitril/Valsartan

SACUBITRIL/VALSARTAN Entresto

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Appendix C. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Outcome in this Request

		Code	
Code	Description	Category	Code Type
	Intensive Care Unit Admission, Intubation, Tracheostomy, or Laryngoscopy		
09HN7BZ	Insertion of Airway into Nasopharynx, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
9HN8BZ	Insertion of Airway into Nasopharynx, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
B110F4	Bypass Trachea to Cutaneous with Tracheostomy Device, Open Approach	Procedure	ICD-10-PCS
0B110Z4	Bypass Trachea to Cutaneous, Open Approach	Procedure	ICD-10-PCS
0B113F4	Bypass Trachea to Cutaneous with Tracheostomy Device, Percutaneous Approach	Procedure	ICD-10-PCS
0B113Z4	Bypass Trachea to Cutaneous, Percutaneous Approach	Procedure	ICD-10-PCS
	Bypass Trachea to Cutaneous with Tracheostomy Device, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0B114F4			
0B114Z4	Bypass Trachea to Cutaneous, Percutaneous Endoscopic Approach		ICD-10-PCS
0B710DZ	Dilation of Trachea with Intraluminal Device, Open Approach	Procedure	ICD-10-PCS
0B710ZZ	Dilation of Trachea, Open Approach	Procedure	ICD-10-PCS
0B713DZ	Dilation of Trachea with Intraluminal Device, Percutaneous Approach	Procedure	ICD-10-PCS
0B713ZZ	Dilation of Trachea, Percutaneous Approach	Procedure	ICD-10-PCS
0B714DZ	Dilation of Trachea with Intraluminal Device, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0B714ZZ	Dilation of Trachea, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0B717DZ	Dilation of Trachea with Intraluminal Device, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0B717ZZ	Dilation of Trachea, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
	Dilation of Trachea with Intraluminal Device, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0B718DZ			
0B718ZZ	Dilation of Trachea, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0B720DZ	Dilation of Carina with Intraluminal Device, Open Approach	Procedure	ICD-10-PCS
0B720ZZ	Dilation of Carina, Open Approach		ICD-10-PCS
0B723DZ	Dilation of Carina with Intraluminal Device, Percutaneous Approach	Procedure	ICD-10-PCS
0B723ZZ	Dilation of Carina, Percutaneous Approach	Procedure	ICD-10-PCS
0B724DZ	Dilation of Carina with Intraluminal Device, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0B724ZZ	Dilation of Carina, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0B727DZ	Dilation of Carina with Intraluminal Device, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0B727ZZ	Dilation of Carina, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
	Dilation of Carina with Intraluminal Device, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0B728DZ			
0B728ZZ	Dilation of Carina, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
	Insertion of Intraluminal Device into Tracheobronchial Tree, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0BH07DZ			
OBH17EZ	Insertion of Endotracheal Airway into Trachea, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
	Insertion of Endotracheal Airway into Trachea, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
OBH18EZ			
OBJ14ZZ	Inspection of Trachea, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
OBJ18ZZ	Inspection of Trachea, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
OBQ10ZZ	Repair Trachea, Open Approach	Procedure	ICD-10-PCS
OBQ13ZZ	Repair Trachea, Percutaneous Approach	Procedure	ICD-10-PCS
OBQ14ZZ	Repair Trachea, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
OBQ17ZZ	Repair Trachea, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
OBQ18ZZ	Repair Trachea, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0BQ20ZZ	Repair Carina, Open Approach	Procedure	ICD-10-PCS
0BQ23ZZ	Repair Carina, Percutaneous Approach	Procedure	ICD-10-PCS
0BQ24ZZ	Repair Carina, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS

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Appendix C. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Outcome in this Request

		Code	
Code	Description	Category	Code Type
OBQ27ZZ	Repair Carina, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0BQ28ZZ	Repair Carina, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0CHY7BZ	Insertion of Airway into Mouth and Throat, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
	Insertion of Airway into Mouth and Throat, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
OCHY8BZ			
0CJS4ZZ	Inspection of Larynx, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
OCJS8ZZ	Inspection of Larynx, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
ODH57BZ	Insertion of Airway into Esophagus, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
ODH58BZ	Insertion of Airway into Esophagus, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
ODL57DZ	Occlusion of Esophagus with Intraluminal Device, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
	Occlusion of Esophagus with Intraluminal Device, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
ODL58DZ			
	Insertion of Other Device into Respiratory Tract, Via Natural or Artificial Opening		ICD-10-PCS
31.1	Tracheostomy	Procedure	ICD-9-CM
31.2	Tracheostomy	Procedure	ICD-9-CM
31.21	Tracheostomy	Procedure	ICD-9-CM
31.29	Tracheostomy	Procedure	ICD-9-CM
31.42	Laryngoscopy	Procedure	ICD-9-CM
31.99	Intubation	Procedure	ICD-9-CM
31231	Laryngoscopy	Procedure	CPT-4
31502	Intubation	Procedure	CPT-4
31505	Laryngoscopy	Procedure	CPT-4
31525	Laryngoscopy	Procedure	CPT-4
31526	Laryngoscopy	Procedure	CPT-4
31527	Laryngoscopy	Procedure	CPT-4
31528	Laryngoscopy	Procedure	CPT-4
31529	Laryngoscopy	Procedure	CPT-4
31560	Laryngoscopy	Procedure	CPT-4
31561	Laryngoscopy	Procedure	CPT-4
31603	Tracheostomy	Procedure	CPT-4
31605	Tracheostomy	Procedure	CPT-4
31610	Tracheostomy	Procedure	CPT-4
31612	Tracheostomy	Procedure	CPT-4
31615	Tracheostomy	Procedure	CPT-4
	Irrigation of Respiratory Tract using Irrigating Substance, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
3E1F78Z			
	Irrigation of Respiratory Tract using Irrigating Substance, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
3E1F88Z	Endoscopic		
5A1935Z	Respiratory Ventilation, Less than 24 Consecutive Hours	Procedure	ICD-10-PCS
5A1945Z	Respiratory Ventilation, 24-96 Consecutive Hours		ICD-10-PCS
5A1955Z	Respiratory Ventilation, Greater than 96 Consecutive Hours	Procedure	ICD-10-PCS
91000	Intubation	Procedure	CPT-4
96	Intubation		ICD-9-CM
96.0	Intubation		ICD-9-CM
96.01	Intubation		ICD-9-CM
96.02	Intubation		ICD-9-CM
96.03	Intubation	Procedure	ICD-9-CM

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Appendix C. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Outcome in this Request

		Code	
Code	Description	Category	Code Type
96.04	Intubation	Procedure	ICD-9-CM
96.05	Intubation	Procedure	ICD-9-CM
96.06	Intubation	Procedure	ICD-9-CM
96.56	Intubation	Procedure	ICD-9-CM
96.7	Intubation	Procedure	ICD-9-CM
96.70	Intubation	Procedure	ICD-9-CM
96.71	Intubation	Procedure	ICD-9-CM
96.72	Intubation	Procedure	ICD-9-CM
99220	ICU Admission	Procedure	CPT-4
99221	ICU Admission	Procedure	CPT-4
99222	ICU Admission	Procedure	CPT-4
99223	ICU Admission	Procedure	CPT-4
99224	ICU Admission	Procedure	CPT-4
99225	ICU Admission	Procedure	CPT-4
99226	ICU Admission	Procedure	CPT-4
99291	ICU Admission	Procedure	CPT-4
99292	ICU Admission	Procedure	CPT-4
A0396	Intubation	Procedure	HCPCS
V44.0	Tracheostomy	Diagnosis	ICD-9-CM
V55.0	Tracheostomy	Diagnosis	ICD-9-CM
Z43.0	Encounter for Attention to Tracheostomy	Diagnosis	ICD-10-CM
Z93.0	Tracheostomy Status	Diagnosis	ICD-10-CM
	Angioedema		
995.1	Angioedema	Diagnosis	ICD-9-CM
T783XXA	Angioedema	Diagnosis	ICD-10-CM

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Appendix D. Generic and Brand Names of Medical Products Used to Define Exposure Incidence and Exclusion Criteria in this Request

Generic Name Brand Name

Angiotensin-Converting Enzyme Inhibitors (ACEI)

AMLODIPINE BESYLATE/BENAZEPRIL HCL Lotrel

AMLODIPINE BESYLATE/BENAZEPRIL HCL amlodipine-benazepril

BENAZEPRIL HCL Lotensin
BENAZEPRIL HCL
BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE Lotensin HCT

BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE benazepril-hydrochlorothiazide

CAPTOPRIL captopril

CAPTOPRIL/HYDROCHLOROTHIAZIDE captopril-hydrochlorothiazide

ENALAPRIL MALEATE Epaned ENALAPRIL MALEATE Vasotec

ENALAPRIL MALEATE enalapril maleate

ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE Vaseretic

ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE enalapril-hydrochlorothiazide

FOSINOPRIL SODIUM fosinopril

FOSINOPRIL SODIUM/HYDROCHLOROTHIAZIDE fosinopril-hydrochlorothiazide

LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL
LISINOPRIL/HYDROCHLOROTHIAZIDE

Prinivil
Qbrelis
Zestril
LISINOPRIL
LISINOPRIL
Zestoretic

LISINOPRIL/HYDROCHLOROTHIAZIDE lisinopril-hydrochlorothiazide

MOEXIPRIL HCL Univasc
MOEXIPRIL HCL moexipril
MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE Uniretic

MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE moexipril-hydrochlorothiazide

PERINDOPRIL ARGININE/AMLODIPINE BESYLATE Prestalia
PERINDOPRIL ERBUMINE Aceon

PERINDOPRIL ERBUMINE perindopril erbumine

QUINAPRIL HCL Accupril
QUINAPRIL HCL quinapril
QUINAPRIL HCL/HYDROCHLOROTHIAZIDE Accuretic

QUINAPRIL HCL/HYDROCHLOROTHIAZIDE quinapril-hydrochlorothiazide

RAMIPRIL Altace
RAMIPRIL ramipril
TRANDOLAPRIL Mavik
TRANDOLAPRIL trandolapril
TRANDOLAPRIL/VERAPAMIL HCL Tarka

TRANDOLAPRIL/VERAPAMIL HCL trandolapril-verapamil amlodipine besylate/benazepril HCl amlodipine-benazepril

benazepril HCl Lotensin
benazepril HCl benazepril
captopril captopril

enalapril maleate enalapril maleate

lisinopril lisinopril/hydrochlorothiazide lisinopril-hydrochlorothiazide

quinapril HCl quinapril ramipril ramolapril trandolapril trandolapril

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Appendix D. Generic and Brand Names of Medical Products Used to Define Exposure Incidence and Exclusion Criteria in this Request

Generic Name Brand Name

Angiotensin II Receptor Blockers (ARB)

AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL Azor

AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL amlodipine-olmesartan

AMLODIPINE BESYLATE/VALSARTAN Exforge

AMLODIPINE BESYLATE/VALSARTAN amlodipine-valsartan

AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE Exforge HCT

AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE amlodipine-valsartan-hcthiazid

AZILSARTAN MEDOXOMIL
AZILSARTAN MEDOXOMIL/CHLORTHALIDONE
CANDESARTAN CILEXETIL
CANDESARTAN CILEXETIL
CANDESARTAN CILEXETIL
CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE
Atacand HCT

CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE candesartan-hydrochlorothiazid

EPROSARTAN MESYLATE
EPROSARTAN MESYLATE
EPROSARTAN MESYLATE/HYDROCHLOROTHIAZIDE
IRBESARTAN
IRBESARTAN
IRBESARTAN
IRBESARTAN/HYDROCHLOROTHIAZIDE
EPROSARTAN/HYDROCHLOROTHIAZIDE
IRBESARTAN
IRBESARTAN/HYDROCHLOROTHIAZIDE
Teveten
eprosartan
Avapro
irbesartan
Avalide

IRBESARTAN/HYDROCHLOROTHIAZIDE irbesartan-hydrochlorothiazide

LOSARTAN POTASSIUM Cozaar LOSARTAN POTASSIUM losartan LOSARTAN Hyzaar

POTASSIUM/HYDROCHLOROTHIAZIDE

LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE losartan-hydrochlorothiazide

NEBIVOLOL HCL/VALSARTAN

OLMESARTAN MEDOXOMIL

OLMESARTAN MEDOXOMIL

OLMESARTAN MEDOXOMIL

OLMESARTAN MEDOXOMIL/AMLODIPINE

Tribenzor

BESYLATE/HYDROCHLOROTHIAZIDE

OLMESARTAN MEDOXOMIL/AMLODIPINE olmesartan-amlodipin-hcthiazid

BESYLATE/HYDROCHLOROTHIAZIDE

OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE Benicar HCT

OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE olmesartan-hydrochlorothiazide

TELMISARTAN Micardis
TELMISARTAN telmisartan
TELMISARTAN/AMLODIPINE BESYLATE Twynsta

TELMISARTAN/AMLODIPINE BESYLATE telmisartan-amlodipine

TELMISARTAN/HYDROCHLOROTHIAZIDE Micardis HCT

TELMISARTAN/HYDROCHLOROTHIAZIDE telmisartan-hydrochlorothiazid

VALSARTAN Diovan
VALSARTAN valsartan
VALSARTAN/HYDROCHLOROTHIAZIDE Diovan HCT

VALSARTAN/HYDROCHLOROTHIAZIDE valsartan-hydrochlorothiazide amlodipine besylate/olmesartan medoxomil amlodipine-olmesartan amlodipine-valsartan

amlodipine besylate/valsartan/hydrochlorothiazide amlodipine-valsartan-hcthiazid

candesartan cilexetil Atacand candesartan cilexetil candesartan cilexetil/hydrochlorothiazide Atacand HCT

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Appendix D. Generic and Brand Names of Medical Products Used to Define Exposure Incidence and Exclusion Criteria in this Request

Generic Name

candesartan cilexetil/hydrochlorothiazide

irbesartan

irbesartan/hydrochlorothiazide

losartan potassium

losartan potassium/hydrochlorothiazide

olmesartan medoxomil olmesartan medoxomil

olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide

olmesartan medoxomil/hydrochlorothiazide

telmisartan

telmisartan/hydrochlorothiazide

valsartan

valsartan/hydrochlorothiazide

Brand Name

candesartan-hydrochlorothiazid

irbesartan

irbesartan-hydrochlorothiazide

losartan

losartan-hydrochlorothiazide

Benicar olmesartan

olmesartan-amlodipin-hcthiazid

Benicar HCT telmisartan

telmisartan-hydrochlorothiazid

valsartan

valsartan-hydrochlorothiazide

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Appendix E. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Inclusion Criteria in this Request

Code	Description	Code Category	Code Type
	Heart Failure		
402.01	Malignant hypertensive heart disease with heart failure	Diagnosis	ICD-9-CM
402.11	Benign hypertensive heart disease with heart failure	Diagnosis	ICD-9-CM
402.91	Hypertensive heart disease, unspecified, with heart failure	Diagnosis	ICD-9-CM
	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic	Diagnosis	ICD-9-CM
404.01	kidney disease stage I through stage IV, or unspecified		
	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic	Diagnosis	ICD-9-CM
404.03	kidney disease stage V or end stage renal disease		
10111	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic	Diagnosis	ICD-9-CM
404.11	kidney disease stage I through stage IV, or unspecified		100 0 014
404.42	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney	Diagnosis	ICD-9-CM
404.13	disease stage V or end stage renal disease		
404.04	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with	Diagnosis	ICD-9-CM
404.91	chronic kidney disease stage I through stage IV, or unspecified	5	100 0 014
404.02	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic	Diagnosis	ICD-9-CM
404.93	kidney disease stage V or end stage renal disease	Di	100 0 014
428	Heart failure	Diagnosis	ICD-9-CM
428.0 428.1	Congestive heart failure, unspecified	Diagnosis	ICD-9-CM
428.1	Left heart failure Systolic heart failure	Diagnosis	ICD-9-CM
428.20	,	Diagnosis	ICD-9-CM
428.21	Unspecified systolic heart failure Acute systolic heart failure	Diagnosis Diagnosis	ICD-9-CM ICD-9-CM
428.22	Chronic systolic heart failure	_	ICD-9-CIVI
428.23	Acute on chronic systolic heart failure	Diagnosis Diagnosis	ICD-9-CIVI
428.23	Diastolic heart failure	Diagnosis	ICD-9-CIVI
428.30	Unspecified diastolic heart failure	Diagnosis	ICD-9-CM
428.31	Acute diastolic heart failure	Diagnosis	ICD-9-CM
428.32	Chronic diastolic heart failure	Diagnosis	ICD-9-CM
428.33	Acute on chronic diastolic heart failure	Diagnosis	ICD-9-CM
428.4	Combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.40	Unspecified combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.41	Acute combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.42	Chronic combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.43	Acute on chronic combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.9	Unspecified heart failure	Diagnosis	ICD-9-CM
111.0	Hypertensive heart disease with heart failure	Diagnosis	ICD-10-CM
	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4	Diagnosis	ICD-10-CM
113.0	chronic kidney disease, or unspecified chronic kidney disease		
	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic	Diagnosis	ICD-10-CM
113.2	kidney disease, or end stage renal disease		
150	Heart failure	Diagnosis	ICD-10-CM
150.1	Left ventricular failure, unspecified	Diagnosis	ICD-10-CM
150.2	Systolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.20	Unspecified systolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.21	Acute systolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.22	Chronic systolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.23	Acute on chronic systolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.3	Diastolic (congestive) heart failure	Diagnosis	ICD-10-CM

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Appendix E. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Inclusion Criteria in this Request

		Code	
Code	Description	Category	Code Type
150.30	Unspecified diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.31	Acute diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.32	Chronic diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.33	Acute on chronic diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.4	Combined systolic (congestive) and diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.810	Right heart failure, unspecified	Diagnosis	ICD-10-CM
150.811	Acute right heart failure	Diagnosis	ICD-10-CM
150.812	Chronic right heart failure	Diagnosis	ICD-10-CM
150.813	Acute on chronic right heart failure	Diagnosis	ICD-10-CM
150.814	Right heart failure due to left heart failure	Diagnosis	ICD-10-CM
150.82	Biventricular heart failure	Diagnosis	ICD-10-CM
150.83	High output heart failure	Diagnosis	ICD-10-CM
150.84	End stage heart failure	Diagnosis	ICD-10-CM
150.89	Other heart failure	Diagnosis	ICD-10-CM
150.9	Heart failure, unspecified	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
	Allergies		
472.0	Chronic rhinitis	Diagnosis	ICD-9-CM
477.0	Allergic rhinitis due to pollen	Diagnosis	ICD-9-CM
477.1	Allergic rhinitis, due to food	Diagnosis	ICD-9-CM
477.2	Allergic rhinitis due to animal (cat) (dog) hair and dander	Diagnosis	ICD-9-CM
477.8	Allergic rhinitis due to other allergen	Diagnosis	ICD-9-CM
477.9	Allergic rhinitis, cause unspecified	Diagnosis	ICD-9-CM
478.8	Upper respiratory tract hypersensitivity reaction, site unspecified	Diagnosis	ICD-9-CM
558.3	Gastroenteritis and colitis, allergic	Diagnosis	ICD-9-CM
691.0	Diaper or napkin rash	Diagnosis	ICD-9-CM
691.8	Other atopic dermatitis and related conditions	Diagnosis	ICD-9-CM
692.0	Contact dermatitis and other eczema due to detergents	Diagnosis	ICD-9-CM
692.1	Contact dermatitis and other eczema due to oils and greases	Diagnosis	ICD-9-CM
692.2	Contact dermatitis and other eczema due to solvents	Diagnosis	ICD-9-CM
692.3	Contact dermatitis and other eczema due to drugs and medicines in contact with skin	Diagnosis	ICD-9-CM
692.4	Contact dermatitis and other eczema due to other chemical products	Diagnosis	ICD-9-CM
692.5	Contact dermatitis and other eczema due to food in contact with skin	Diagnosis	ICD-9-CM
692.6	Contact dermatitis and other eczema due to plants (except food)	Diagnosis	ICD-9-CM
692.70	Unspecified dermatitis due to sun	Diagnosis	ICD-9-CM
692.71	Contact dermatitis and other eczema due to sunburn	Diagnosis	ICD-9-CM
692.72	Acute dermatitis due to solar radiation	Diagnosis	ICD-9-CM
692.73	Actinic reticuloid and actinic granuloma	Diagnosis	ICD-9-CM
692.74	Other chronic dermatitis due to solar radiation	Diagnosis	ICD-9-CM
692.75	Disseminated superficial actinic porokeratosis (DSAP)	Diagnosis	ICD-9-CM
692.76	Sunburn of second degree	Diagnosis	ICD-9-CM
692.77	Sunburn of third degree	Diagnosis	ICD-9-CM
692.79	Other dermatitis due to solar radiation	Diagnosis	ICD-9-CM
692.81	Dermatitis due to cosmetics	Diagnosis	ICD-9-CM
692.82	Dermatitis due to other radiation	Diagnosis	ICD-9-CM
692.83	Dermatitis due to metals	Diagnosis	ICD-9-CM
692.84	Contact dermatitis and other eczema due to animal (cat) (dog) dander	Diagnosis	ICD-9-CM
692.89	Contact dermatitis and other eczema due to other specified agent	Diagnosis	ICD-9-CM
692.9	Contact dermatitis and other eczema, due to unspecified cause	Diagnosis	ICD-9-CM
693.0	Dermatitis due to drugs and medicines taken internally	Diagnosis	ICD-9-CM
693.1	Dermatitis due to food taken internally	Diagnosis	ICD-9-CM
693.8	Dermatitis due to other specified substances taken internally	Diagnosis	ICD-9-CM
693.9	Dermatitis due to unspecified substance taken internally	Diagnosis	ICD-9-CM
708.0	Allergic urticaria	Diagnosis	ICD-9-CM
708.1	Idiopathic urticaria	Diagnosis	ICD-9-CM
708.2	Urticaria due to cold and heat	Diagnosis	ICD-9-CM
708.3	Dermatographic urticaria	Diagnosis	ICD-9-CM
708.4	Vibratory urticaria	Diagnosis	ICD-9-CM
708.5	Cholinergic urticaria	Diagnosis	ICD-9-CM
708.8	Other specified urticaria	Diagnosis	ICD-9-CM
708.9	Unspecified urticaria	Diagnosis	ICD-9-CM
995.0	Other anaphylactic reaction	Diagnosis	ICD-9-CM

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		Code	
Code	Description	Category	Code Type
995.27	Other drug allergy	Diagnosis	ICD-9-CM
995.3	Allergy, unspecified not elsewhere classified	Diagnosis	ICD-9-CM
995.7	Other adverse food reactions, not elsewhere classified	Diagnosis	ICD-9-CM
J30.0	Vasomotor rhinitis	Diagnosis	ICD-10-CM
J30.1	Allergic rhinitis due to pollen	Diagnosis	ICD-10-CM
J30.2	Other seasonal allergic rhinitis	Diagnosis	ICD-10-CM
J30.5	Allergic rhinitis due to food	Diagnosis	ICD-10-CM
J30.81	Allergic rhinitis due to animal (cat) (dog) hair and dander	Diagnosis	ICD-10-CM
J30.89	Other allergic rhinitis	Diagnosis	ICD-10-CM
J30.9	Allergic rhinitis, unspecified	Diagnosis	ICD-10-CM
J31.0	Chronic rhinitis	Diagnosis	ICD-10-CM
J39.3	Upper respiratory tract hypersensitivity reaction, site unspecified	Diagnosis	ICD-10-CM
K52.21	Food protein-induced enterocolitis syndrome	Diagnosis	ICD-10-CM
K52.22	Food protein-induced enteropathy	Diagnosis	ICD-10-CM
K52.29	Other allergic and dietetic gastroenteritis and colitis	Diagnosis	ICD-10-CM
L20.0	Besnier's prurigo	Diagnosis	ICD-10-CM
L20.81	Atopic neurodermatitis	Diagnosis	ICD-10-CM
L20.82	Flexural eczema	Diagnosis	ICD-10-CM
L20.84	Intrinsic (allergic) eczema	Diagnosis	ICD-10-CM
L20.89	Other atopic dermatitis	Diagnosis	ICD-10-CM
L20.9	Atopic dermatitis, unspecified	Diagnosis	ICD-10-CM
L22	Diaper dermatitis	Diagnosis	ICD-10-CM
L23.0	Allergic contact dermatitis due to metals	Diagnosis	ICD-10-CM
L23.1	Allergic contact dermatitis due to adhesives	Diagnosis	ICD-10-CM
L23.2	Allergic contact dermatitis due to cosmetics	Diagnosis	ICD-10-CM
L23.3	Allergic contact dermatitis due to drugs in contact with skin	Diagnosis	ICD-10-CM
L23.4	Allergic contact dermatitis due to dyes	Diagnosis	ICD-10-CM
L23.5	Allergic contact dermatitis due to other chemical products	Diagnosis	ICD-10-CM
L23.6	Allergic contact dermatitis due to food in contact with the skin	Diagnosis	ICD-10-CM
L23.7	Allergic contact dermatitis due to plants, except food	Diagnosis	ICD-10-CM
L23.81	Allergic contact dermatitis due to animal (cat) (dog) dander	Diagnosis	ICD-10-CM
L23.89	Allergic contact dermatitis due to other agents	Diagnosis	ICD-10-CM
L23.9	Allergic contact dermatitis, unspecified cause	Diagnosis	ICD-10-CM
L24.0	Irritant contact dermatitis due to detergents	Diagnosis	ICD-10-CM
L24.1	Irritant contact dermatitis due to oils and greases	Diagnosis	ICD-10-CM
L24.2	Irritant contact dermatitis due to solvents	Diagnosis	ICD-10-CM
L24.3	Irritant contact dermatitis due to cosmetics	Diagnosis	ICD-10-CM
L24.4	Irritant contact dermatitis due to drugs in contact with skin	Diagnosis	ICD-10-CM
L24.5	Irritant contact dermatitis due to other chemical products	Diagnosis	ICD-10-CM
L24.6	Irritant contact dermatitis due to food in contact with skin	Diagnosis	ICD-10-CM
L24.7	Irritant contact dermatitis due to plants, except food	Diagnosis	ICD-10-CM
L24.81	Irritant contact dermatitis due to metals	Diagnosis	ICD-10-CM
L24.89	Irritant contact dermatitis due to other agents	Diagnosis	ICD-10-CM
L24.9	Irritant contact dermatitis, unspecified cause	Diagnosis	ICD-10-CM
L25.0	Unspecified contact dermatitis due to cosmetics	Diagnosis	ICD-10-CM
L25.1	Unspecified contact dermatitis due to drugs in contact with skin	Diagnosis	ICD-10-CM
L25.2	Unspecified contact dermatitis due to dyes	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
L25.3	Unspecified contact dermatitis due to other chemical products	Diagnosis	ICD-10-CM
L25.4	Unspecified contact dermatitis due to food in contact with skin	Diagnosis	ICD-10-CM
L25.5	Unspecified contact dermatitis due to plants, except food	Diagnosis	ICD-10-CM
L25.8	Unspecified contact dermatitis due to other agents	Diagnosis	ICD-10-CM
L25.9	Unspecified contact dermatitis, unspecified cause	Diagnosis	ICD-10-CM
L27.0	Generalized skin eruption due to drugs and medicaments taken internally	Diagnosis	ICD-10-CM
L27.1	Localized skin eruption due to drugs and medicaments taken internally	Diagnosis	ICD-10-CM
L27.2	Dermatitis due to ingested food	Diagnosis	ICD-10-CM
L27.8	Dermatitis due to other substances taken internally	Diagnosis	ICD-10-CM
L27.9	Dermatitis due to unspecified substance taken internally	Diagnosis	ICD-10-CM
L50.0	Allergic urticaria	Diagnosis	ICD-10-CM
L50.1	Idiopathic urticaria	Diagnosis	ICD-10-CM
L50.2	Urticaria due to cold and heat	Diagnosis	ICD-10-CM
L50.3	Dermatographic urticaria	Diagnosis	ICD-10-CM
L50.4	Vibratory urticaria	Diagnosis	ICD-10-CM
L50.5	Cholinergic urticaria	Diagnosis	ICD-10-CM
L50.6	Contact urticaria	Diagnosis	ICD-10-CM
L50.8	Other urticaria	Diagnosis	ICD-10-CM
L50.9	Urticaria, unspecified	Diagnosis	ICD-10-CM
L55.0	Sunburn of first degree	Diagnosis	ICD-10-CM
L55.1	Sunburn of second degree	Diagnosis	ICD-10-CM
L55.2	Sunburn of third degree	Diagnosis	ICD-10-CM
L55.9	Sunburn, unspecified	Diagnosis	ICD-10-CM
L56.0	Drug phototoxic response	Diagnosis	ICD-10-CM
L56.1	Drug photoallergic response	Diagnosis	ICD-10-CM
L56.2	Photocontact dermatitis [berloque dermatitis]	Diagnosis	ICD-10-CM
L56.3	Solar urticaria	Diagnosis	ICD-10-CM
L56.4	Polymorphous light eruption	Diagnosis	ICD-10-CM
L56.5	Disseminated superficial actinic porokeratosis (DSAP)	Diagnosis	ICD-10-CM
L56.8	Other specified acute skin changes due to ultraviolet radiation	Diagnosis	ICD-10-CM
L56.9	Acute skin change due to ultraviolet radiation, unspecified	Diagnosis	ICD-10-CM
L57.1	Actinic reticuloid	Diagnosis	ICD-10-CM
L57.5	Actinic granuloma	Diagnosis	ICD-10-CM
L57.8	Other skin changes due to chronic exposure to nonionizing radiation	Diagnosis	ICD-10-CM
L57.9	Skin changes due to chronic exposure to nonionizing radiation, unspecified	Diagnosis	ICD-10-CM
L58.0	Acute radiodermatitis	Diagnosis	ICD-10-CM
L58.1	Chronic radiodermatitis	Diagnosis	ICD-10-CM
L58.9	Radiodermatitis, unspecified	Diagnosis	ICD-10-CM
T50.995A	Adverse effect of other drugs, medicaments and biological substances, initial encounter	Diagnosis	ICD-10-CM
T78.0	Anaphylactic reaction due to food	Diagnosis	ICD-10-CM
T78.00	Anaphylactic reaction due to unspecified food	Diagnosis	ICD-10-CM
T78.00XA	Anaphylactic reaction due to unspecified food, initial encounter	Diagnosis	ICD-10-CM
T78.00XD	Anaphylactic reaction due to unspecified food, subsequent encounter	Diagnosis	ICD-10-CM
T78.00XS	Anaphylactic reaction due to unspecified food, sequela	Diagnosis	ICD-10-CM
T78.01	Anaphylactic reaction due to peanuts	Diagnosis	ICD-10-CM
T78.01XA	Anaphylactic reaction due to peanuts, initial encounter	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
T78.01XD	Anaphylactic reaction due to peanuts, subsequent encounter	Diagnosis	ICD-10-CM
T78.01XS	Anaphylactic reaction due to peanuts, sequela	Diagnosis	ICD-10-CM
T78.02	Anaphylactic reaction due to shellfish (crustaceans)	Diagnosis	ICD-10-CM
T78.02XA	Anaphylactic reaction due to shellfish (crustaceans), initial encounter	Diagnosis	ICD-10-CM
T78.02XD	Anaphylactic reaction due to shellfish (crustaceans), subsequent encounter	Diagnosis	ICD-10-CM
T78.02XS	Anaphylactic reaction due to shellfish (crustaceans), sequela	Diagnosis	ICD-10-CM
T78.03	Anaphylactic reaction due to other fish	Diagnosis	ICD-10-CM
T78.03XA	Anaphylactic reaction due to other fish, initial encounter	Diagnosis	ICD-10-CM
T78.03XD	Anaphylactic reaction due to other fish, subsequent encounter	Diagnosis	ICD-10-CM
T78.03XS	Anaphylactic reaction due to other fish, sequela	Diagnosis	ICD-10-CM
T78.04	Anaphylactic reaction due to fruits and vegetables	Diagnosis	ICD-10-CM
T78.04XA	Anaphylactic reaction due to fruits and vegetables, initial encounter	Diagnosis	ICD-10-CM
T78.04XD	Anaphylactic reaction due to fruits and vegetables, subsequent encounter	Diagnosis	ICD-10-CM
T78.04XS	Anaphylactic reaction due to fruits and vegetables, sequela	Diagnosis	ICD-10-CM
T78.05	Anaphylactic reaction due to tree nuts and seeds	Diagnosis	ICD-10-CM
T78.05XA	Anaphylactic reaction due to tree nuts and seeds, initial encounter	Diagnosis	ICD-10-CM
T78.05XD	Anaphylactic reaction due to tree nuts and seeds, subsequent encounter	Diagnosis	ICD-10-CM
T78.05XS	Anaphylactic reaction due to tree nuts and seeds, sequela	Diagnosis	ICD-10-CM
T78.06	Anaphylactic reaction due to food additives	Diagnosis	ICD-10-CM
T78.06XA	Anaphylactic reaction due to food additives, initial encounter	Diagnosis	ICD-10-CM
T78.06XD	Anaphylactic reaction due to food additives, subsequent encounter	Diagnosis	ICD-10-CM
T78.06XS	Anaphylactic reaction due to food additives, sequela	Diagnosis	ICD-10-CM
T78.07	Anaphylactic reaction due to milk and dairy products	Diagnosis	ICD-10-CM
T78.07XA	Anaphylactic reaction due to milk and dairy products, initial encounter	Diagnosis	ICD-10-CM
T78.07XD	Anaphylactic reaction due to milk and dairy products, subsequent encounter	Diagnosis	ICD-10-CM
T78.07XS	Anaphylactic reaction due to milk and dairy products, sequela	Diagnosis	ICD-10-CM
T78.08	Anaphylactic reaction due to eggs	Diagnosis	ICD-10-CM
T78.08XA	Anaphylactic reaction due to eggs, initial encounter	Diagnosis	ICD-10-CM
T78.08XD	Anaphylactic reaction due to eggs, subsequent encounter	Diagnosis	ICD-10-CM
T78.08XS	Anaphylactic reaction due to eggs, sequela	Diagnosis	ICD-10-CM
T78.09	Anaphylactic reaction due to other food products	Diagnosis	ICD-10-CM
T78.09XA	Anaphylactic reaction due to other food products, initial encounter	Diagnosis	ICD-10-CM
T78.09XD	Anaphylactic reaction due to other food products, subsequent encounter	Diagnosis	ICD-10-CM
T78.09XS	Anaphylactic reaction due to other food products, sequela	Diagnosis	ICD-10-CM
T78.1XXA	Other adverse food reactions, not elsewhere classified, initial encounter	Diagnosis	ICD-10-CM
T78.2	Anaphylactic shock, unspecified	Diagnosis	ICD-10-CM
T78.2XXA	Anaphylactic shock, unspecified, initial encounter	Diagnosis	ICD-10-CM
T78.2XXD	Anaphylactic shock, unspecified, subsequent encounter	Diagnosis	ICD-10-CM
T78.2XXS	Anaphylactic shock, unspecified, sequela	Diagnosis	ICD-10-CM
T78.40	Allergy, unspecified	Diagnosis	ICD-10-CM
T78.40XA	Allergy, unspecified, initial encounter	Diagnosis	ICD-10-CM
T78.40XD	Allergy, unspecified, subsequent encounter	Diagnosis	ICD-10-CM
T78.40XS	Allergy, unspecified, sequela	Diagnosis	ICD-10-CM
T78.49XA	Other allergy, initial encounter	Diagnosis	ICD-10-CM
T80.5	Anaphylactic reaction due to serum	Diagnosis	ICD-10-CM
T80.51	Anaphylactic reaction due to administration of blood and blood products	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
T80.51XA	Anaphylactic reaction due to administration of blood and blood products, initial encounter	Diagnosis	ICD-10-CM
T80.51XD	Anaphylactic reaction due to administration of blood and blood products, subsequent	Diagnosis	ICD-10-CM
T80.51XS	encounter Anaphylactic reaction due to administration of blood and blood products, sequela	Diagnosis	ICD-10-CM
T80.51A3	Anaphylactic reaction due to administration of blood and blood products, sequela	Diagnosis	ICD-10-CM
T80.52XA	Anaphylactic reaction due to vaccination Anaphylactic reaction due to vaccination, initial encounter	Diagnosis	ICD-10-CM
T80.52XA	Anaphylactic reaction due to vaccination, initial encounter Anaphylactic reaction due to vaccination, subsequent encounter	Diagnosis	ICD-10-CIVI
T80.52XS	Anaphylactic reaction due to vaccination, subsequent encounter Anaphylactic reaction due to vaccination, sequela	Diagnosis	ICD-10-CM
T80.59	Anaphylactic reaction due to vaccination, sequela	Diagnosis	ICD-10-CM
T80.59XA	Anaphylactic reaction due to other serum, initial encounter	Diagnosis	ICD-10-CM
T80.59XD	Anaphylactic reaction due to other serum, subsequent encounter	Diagnosis	ICD-10-CM
T80.59XS	Anaphylactic reaction due to other serum, sequela	Diagnosis	ICD-10-CM
T88.6	Anaphylactic reaction due to other serum, sequela Anaphylactic reaction due to adverse effect of correct drug or medicament properly	Diagnosis	ICD-10-CM
100.0	administered	Diagnosis	ICD-10-CIVI
T88.6XXA	Anaphylactic reaction due to adverse effect of correct drug or medicament properly	Diagnosis	ICD-10-CM
100.0774	administered, initial encounter	Diagnosis	ICD-10-CIVI
T88.6XXD	Anaphylactic reaction due to adverse effect of correct drug or medicament properly	Diagnosis	ICD-10-CM
100.0770	administered, subsequent	Diagnosis	ICD-10-CIVI
	·		
T88.6XXS	encounter Anaphylactic reaction due to adverse effect of correct drug or medicament properly	Diagnosis	ICD-10-CM
100.0775	administered, sequela	Diagnosis	ICD-10-CIVI
V07.1	Need for desensitization to allergens	Diagnosis	ICD-9-CM
V13.81	Personal history of anaphylaxis	Diagnosis	ICD-9-CM
V13.01 V14.0	Personal history of allergy to penicillin	Diagnosis	ICD-9-CM
V14.1	Personal history of allergy to other antibiotic agent	Diagnosis	ICD-9-CM
V14.2	Personal history of allergy to sulfonamides	Diagnosis	ICD-9-CM
V14.2 V14.3	Personal history of allergy to other anti-infective agent	Diagnosis	ICD-9-CM
V14.4	Personal history of allergy to anesthetic agent	Diagnosis	ICD-9-CM
V14.5	Personal history of allergy to narcotic agent	Diagnosis	ICD-9-CM
V14.6	Personal history of allergy to analgesic agent	Diagnosis	ICD-9-CM
V14.7	Personal history of allergy to serum or vaccine	Diagnosis	ICD-9-CM
V14.8	Personal history of allergy to other specified medicinal agents	Diagnosis	ICD-9-CM
V14.9	Personal history of allergy to unspecified medicinal agent	Diagnosis	ICD-9-CM
V15.09	Personal history of other allergy, other than to medicinal agents	Diagnosis	ICD-9-CM
V72.7	Diagnostic skin and sensitization tests	Diagnosis	ICD-9-CM
Z01.82	Encounter for allergy testing	Diagnosis	ICD-10-CM
Z01.89	Encounter for other specified special examinations	Diagnosis	ICD-10-CM
Z51.6	Encounter for desensitization to allergens	Diagnosis	ICD-10-CM
Z87.892	Personal history of anaphylaxis	Diagnosis	ICD-10-CM
Z88.0	Allergy status to penicillin	Diagnosis	ICD-10-CM
Z88.1	Allergy status to other antibiotic agents status	Diagnosis	ICD-10-CM
Z88.2	Allergy status to sulfonamides status	Diagnosis	ICD-10-CM
Z88.3	Allergy status to other anti-infective agents status	Diagnosis	ICD-10-CM
Z88.4	Allergy status to anesthetic agent status	Diagnosis	ICD-10-CM
Z88.5	Allergy status to narcotic agent status	Diagnosis	ICD-10-CM
Z88.6	Allergy status to analgesic agent status	Diagnosis	ICD-10-CM
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		Code	
Code	Description	Category	Code Type
Z88.7	Allergy status to serum and vaccine status	Diagnosis	ICD-10-CM
Z88.8	Allergy status to other drugs, medicaments and biological substances status	Diagnosis	ICD-10-CM
Z88.9	Allergy status to unspecified drugs, medicaments and biological substances status	Diagnosis	ICD-10-CM
Z91.0	Allergy status, other than to drugs and biological substances	Diagnosis	ICD-10-CM
Z91.01	Food allergy status	Diagnosis	ICD-10-CM
Z91.010	Allergy to peanuts	Diagnosis	ICD-10-CM
Z91.011	Allergy to milk products	Diagnosis	ICD-10-CM
Z91.012	Allergy to eggs	Diagnosis	ICD-10-CM
Z91.013	Allergy to seafood	Diagnosis	ICD-10-CM
Z91.018	Allergy to other foods	Diagnosis	ICD-10-CM
Z91.02	Food additives allergy status	Diagnosis	ICD-10-CM
Z91.03	Insect allergy status	Diagnosis	ICD-10-CM
Z91.030	Bee allergy status	Diagnosis	ICD-10-CM
Z91.038	Other insect allergy status	Diagnosis	ICD-10-CM
Z91.04	Nonmedicinal substance allergy status	Diagnosis	ICD-10-CM
Z91.040	Latex allergy status	Diagnosis	ICD-10-CM
Z91.041	Radiographic dye allergy status	Diagnosis	ICD-10-CM
Z91.048	Other nonmedicinal substance allergy status	Diagnosis	ICD-10-CM
Z91.09	Other allergy status, other than to drugs and biological substances	Diagnosis	ICD-10-CM
	Angioedema		
995.1	Angioedema	Diagnosis	ICD-9-CM
T783XXA	Angioedema	Diagnosis	ICD-10-CM
T783XXD	Angioneurotic edema, sequela	Diagnosis	ICD-10-CM
T783XXS	Angioneurotic edema, subsequent encounter	Diagnosis	ICD-10-CM
	Diabetes		
250	Diabetes mellitus	Diagnosis	ICD-9-CM
250.0	Diabetes mellitus without mention of complication	Diagnosis	ICD-9-CM
250.00	Diabetes mellitus without mention of complication, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.01	Diabetes mellitus without mention of complication, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.02	Diabetes mellitus without mention of complication, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.03	Diabetes mellitus without mention of complication, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.1	Diabetes with ketoacidosis	Diagnosis	ICD-9-CM
250.10	Diabetes with ketoacidosis, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.11	Diabetes with ketoacidosis, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.12	Diabetes with ketoacidosis, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.13	Diabetes with ketoacidosis, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.2	Diabetes with hyperosmolarity	Diagnosis	ICD-9-CM
250.20	Diabetes with hyperosmolarity, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.21	Diabetes with hyperosmolarity, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.22	Diabetes with hyperosmolarity, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.23	Diabetes with hyperosmolarity, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.3	Diabetes with other coma	Diagnosis	ICD-9-CM
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		Code	
Code	Description	Category	Code Type
250.30	Diabetes with other coma, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.31	Diabetes with other coma, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.32	Diabetes with other coma, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.33	Diabetes with other coma, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.4	Diabetes with renal manifestations	Diagnosis	ICD-9-CM
250.40	Diabetes with renal manifestations, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.41	Diabetes with renal manifestations, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.42	Diabetes with renal manifestations, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.43	Diabetes with renal manifestations, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.5	Diabetes with ophthalmic manifestations	Diagnosis	ICD-9-CM
250.50	Diabetes with ophthalmic manifestations, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.51	Diabetes with ophthalmic manifestations, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.52	Diabetes with ophthalmic manifestations, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.53	Diabetes with ophthalmic manifestations, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.6	Diabetes with neurological manifestations	Diagnosis	ICD-9-CM
250.60	Diabetes with neurological manifestations, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.61	Diabetes with neurological manifestations, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.62	Diabetes with neurological manifestations, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.63	Diabetes with neurological manifestations, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.7	Diabetes with peripheral circulatory disorders	Diagnosis	ICD-9-CM
250.70	Diabetes with peripheral circulatory disorders, type II or unspecified type, not stated as uncontrolled	Diagnosis	ICD-9-CM
250.71	Diabetes with peripheral circulatory disorders, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.72	Diabetes with peripheral circulatory disorders, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.73	Diabetes with peripheral circulatory disorders, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.8	Diabetes with other specified manifestations	Diagnosis	ICD-9-CM
250.80	Diabetes with other specified manifestations, type II or unspecified type, not stated as	Diagnosis	ICD-9-CM
250.81	uncontrolled Diabetes with other specified manifestations, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.82	Diabetes with other specified manifestations, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.83	Diabetes with other specified manifestations, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
250.9	Diabetes with unspecified complication	Diagnosis	ICD-9-CM
250.90	Diabetes with unspecified complication, type II or unspecified type, not stated as uncontrolled	_	ICD-9-CM
250.91	Diabetes with unspecified complication, type I [juvenile type], not stated as uncontrolled	Diagnosis	ICD-9-CM
250.92	Diabetes with unspecified complication, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM

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_		Code	
Code	Description		Code Type
250.93	Diabetes with unspecified complication, type I [juvenile type], uncontrolled	Diagnosis	ICD-9-CM
A5500	For diabetics only, fitting (including follow-up), custom preparation and supply of off-the-shelf	Procedure	HCPCS
	depth-inlay shoe manufactured to accommodate multidensity insert(s), per shoe		
A5501	For diabetics only, fitting (including follow-up), custom preparation and supply of shoe molded	Procedure	HCPCS
	from cast(s) of patient's		
	foot (custom molded shoe), per shoe		
A5503	For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom	Procedure	HCPCS
	molded shoe with roller or		
	rigid rocker bottom, per shoe		
A5504	For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom	Procedure	HCPCS
	molded shoe with		
A5505	wedge(s), per shoe For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom	Procedure	HCPCS
A3303	molded shoe with	riocedure	TICFCS
	metatarsal bar, per shoe		
A5506	For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom	Procedure	HCPCS
	molded shoe with off-set		
	heel(s), per shoe		
A5507	For diabetics only, not otherwise specified modification (including fitting) of off-the-shelf	Procedure	HCPCS
	depth-inlay shoe or custom		
A5508	molded shoe, per shoe For diabetics only, deluxe feature of off-the-shelf depth-inlay shoe or custom molded shoe,	Procedure	HCPCS
A3300	per shoe	Trocedure	rici cs
A5510	For diabetics only, direct formed, compression molded to patient's foot without external heat	Procedure	HCPCS
	source, multiple-density		
	insert(s) prefabricated, per shoe		
A5512	For diabetics only, multiple density insert, direct formed, molded to foot after external heat	Procedure	HCPCS
	source of 230 degrees		
	Fahrenheit or higher, total contact with patient's foot, including arch, base layer minimum of		
	1/4 inch material of shore		
A5513	a 35 durome For diabetics only, multiple density insert, custom molded from model of patient's foot, total	Procedure	HCPCS
	contact with patient's foot,		
	including arch, base layer minimum of 3/16 inch material of shore a 35 durometer or higher),		
	includes arch filler and		
	other sh		
E10.10	Type 1 diabetes mellitus with ketoacidosis without coma	Diagnosis	ICD-10-CM
E10.11	Type 1 diabetes mellitus with ketoacidosis with coma	Diagnosis	ICD-10-CM
E10.21 E10.22	Type 1 diabetes mellitus with diabetic nephropathy	Diagnosis	ICD-10-CM ICD-10-CM
E10.22 E10.29	Type 1 diabetes mellitus with diabetic chronic kidney disease Type 1 diabetes mellitus with other diabetic kidney complication	Diagnosis Diagnosis	ICD-10-CM
E10.311	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema	Diagnosis	ICD-10-CM
E10.319	Type 1 diabetes mellitus with unspecified diabetic retinopathy without macular edema	Diagnosis	ICD-10-CM
		-	
E10.3211	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
	right eye		

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		Code	
Code	Description	Category	Code Type
E10.3212	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
	left eye		
E10.3213	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E40 2240	bilateral The 1 dish shape with wild a small factor dish ship action with a small and a small shape with a	Di	ICD 40 CN4
E10.3219	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E10.3291	unspecified eye Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E10.3231	edema, right eye	Diagnosis	ICD-10-CIVI
E10.3292	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
210.3232	edema, left eye	Diagnosis	102 10 0111
E10.3293	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, bilateral	J	
E10.3299	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, unspecified eye		
E10.3311	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, right eye		
E10.3312	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, left eye		
E10.3313	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10 2210	edema, bilateral	Diamonia	ICD 10 CM
E10.3319	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3391	edema, unspecified eye Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
L10.5551	edema, right eye	Diagnosis	ICD-10-CIVI
E10.3392	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, left eye	- 10011011	
E10.3393	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, bilateral	_	
E10.3399	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, unspecified eye		
E10.3411	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, right eye		
E10.3412	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10 2412	edema, left eye	Diamonia	ICD 10 CM
E10.3413	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3419	edema, bilateral Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
L10.3413	edema, unspecified eye	Diagnosis	ICD-10-CIVI
E10.3491	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
210.0 .01	edema, right eye	Diagnosis	100 10 0111
E10.3492	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, left eye	J	
E10.3493	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, bilateral		
E10.3499	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, unspecified eye		

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		Code	
Code	Description	Category	Code Type
E10.3511	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye	Diagnosis	ICD-10-CM
E10.3512	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye	Diagnosis	ICD-10-CM
E10.3513	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral	Diagnosis	ICD-10-CM
E10.3519	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye	Diagnosis	ICD-10-CM
E10.3521	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E10.3522	right eye Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E10.3523	left eve Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E10.3529	bilateral Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E10.3531	unspecified eve Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E10.3532	macula, right eve Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E10.3533	macula, left eye Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E10.3539	macula, bilateral Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E10.3541	macula, unspecified eye Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and	Diagnosis	ICD-10-CM
E10.3542	rhegmatogenous retinal detachment. right eve Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and	Diagnosis	ICD-10-CM
E10.3543	rhegmatogenous retinal detachment, left eye Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and	Diagnosis	ICD-10-CM
E10.3549	rhegmatogenous retinal detachment, bilateral Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and	Diagnosis	ICD-10-CM
E10.3551 E10.3552 E10.3553	rhegmatogenous retinal detachment, unspecified eye Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	Diagnosis Diagnosis Diagnosis	ICD-10-CM ICD-10-CM ICD-10-CM

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Code	Description	Code Category	Code Type
E10.3559	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye	Diagnosis	ICD-10-CM
E10.3591	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye	Diagnosis	ICD-10-CM
E10.3592	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left	Diagnosis	ICD-10-CM
E10.3593	eye Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral	Diagnosis	ICD-10-CM
E10.3599	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye	Diagnosis	ICD-10-CM
E10.36	Type 1 diabetes mellitus with diabetic cataract	Diagnosis	ICD-10-CM
E10.37X1	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye	_	ICD-10-CM
E10.37X2	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye	Diagnosis	ICD-10-CM
E10.37X3	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral	Diagnosis	ICD-10-CM
E10.37X9	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye	Diagnosis	ICD-10-CM
E10.39	Type 1 diabetes mellitus with other diabetic ophthalmic complication	Diagnosis	ICD-10-CM
E10.40	Type 1 diabetes mellitus with diabetic neuropathy, unspecified	Diagnosis	ICD-10-CM
E10.41	Type 1 diabetes mellitus with diabetic mononeuropathy	Diagnosis	ICD-10-CM
E10.42	Type 1 diabetes mellitus with diabetic polyneuropathy	Diagnosis	ICD-10-CM
E10.43	Type 1 diabetes mellitus with diabetic autonomic (poly)neuropathy	Diagnosis	ICD-10-CM
E10.44	Type 1 diabetes mellitus with diabetic amyotrophy	Diagnosis	ICD-10-CM
E10.49	Type 1 diabetes mellitus with other diabetic neurological complication	Diagnosis	ICD-10-CM
E10.51	Type 1 diabetes mellitus with diabetic peripheral angiopathy without gangrene	Diagnosis	ICD-10-CM
E10.52	Type 1 diabetes mellitus with diabetic peripheral angiopathy with gangrene	Diagnosis	ICD-10-CM
E10.59	Type 1 diabetes mellitus with other circulatory complications	Diagnosis	ICD-10-CM
E10.610	Type 1 diabetes mellitus with diabetic neuropathic arthropathy	Diagnosis	ICD-10-CM
E10.618	Type 1 diabetes mellitus with other diabetic arthropathy	Diagnosis	ICD-10-CM
E10.620	Type 1 diabetes mellitus with diabetic dermatitis	Diagnosis	ICD-10-CM
E10.621	Type 1 diabetes mellitus with foot ulcer	Diagnosis	ICD-10-CM
E10.622	Type 1 diabetes mellitus with other skin ulcer	Diagnosis	ICD-10-CM
E10.628	Type 1 diabetes mellitus with other skin complications	Diagnosis	ICD-10-CM
E10.630	Type 1 diabetes mellitus with periodontal disease	Diagnosis	ICD-10-CM
E10.638	Type 1 diabetes mellitus with other oral complications	Diagnosis	ICD-10-CM
E10.641	Type 1 diabetes mellitus with hypoglycemia with coma	Diagnosis	ICD-10-CM
E10.649	Type 1 diabetes mellitus with hypoglycemia without coma	Diagnosis	ICD-10-CM
E10.65	Type 1 diabetes mellitus with hyperglycemia	Diagnosis	ICD-10-CM
E10.69	Type 1 diabetes mellitus with other specified complication	Diagnosis	ICD-10-CM
E10.8	Type 1 diabetes mellitus with unspecified complications	Diagnosis	ICD-10-CM
E10.9	Type 1 diabetes mellitus without complications	Diagnosis	ICD-10-CM
E11.00	Type 2 diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic- hyperosmolar coma (NKHHC)	Diagnosis	ICD-10-CM
E11.01	Type 2 diabetes mellitus with hyperosmolarity with coma	Diagnosis	ICD-10-CM
E11.21	Type 2 diabetes mellitus with diabetic nephropathy	Diagnosis	ICD-10-CM
L11.Z1	Type 2 diabetes memas with diabetic nephropathy	Diagnosis	ICD TO-CIVI

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		Code	
Code	Description	Category	Code Type
E11.22	Type 2 diabetes mellitus with diabetic chronic kidney disease	Diagnosis	ICD-10-CM
E11.29	Type 2 diabetes mellitus with other diabetic kidney complication	Diagnosis	ICD-10-CM
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema	Diagnosis	ICD-10-CM
E11.319	Type 2 diabetes mellitus with unspecified diabetic retinopathy without macular edema	Diagnosis	ICD-10-CM
E11.3211	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
	right eye		
E11.3212	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E44 0040	left eye		100 10 011
E11.3213	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E44 2240	bilateral	Di	ICD 40 CN4
E11.3219	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E11.3291	unspecified eye Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
L11.3291	edema, right eye	Diagnosis	ICD-10-CIVI
E11.3292	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
L11.3232	edema, left eye	Diagnosis	ICD-10-CIVI
E11.3293	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, bilateral	2.0000.0	.02 20 0
E11.3299	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, unspecified eye	J	
E11.3311	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, right eye		
E11.3312	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, left eye		
E11.3313	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, bilateral		
E11.3319	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, unspecified eye		
E11.3391	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E44 2202	edema, right eye	5	100 40 614
E11.3392	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3393	edema, left eye	Diagnosis	ICD-10-CM
E11.3393	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral	Diagnosis	ICD-10-CIVI
E11.3399	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
L11.3333	edema, unspecified eye	Diagnosis	ICD-10-CIVI
E11.3411	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, right eye	- 100110110	
E11.3412	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, left eye	J	
E11.3413	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, bilateral		
E11.3419	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, unspecified eye		
E11.3491	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, right eye		

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		Code	
Code	Description	Category	Code Type
E11.3492	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3493	edema, left eye Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral	Diagnosis	ICD-10-CM
E11.3499	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye	Diagnosis	ICD-10-CM
E11.3511	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye	Diagnosis	ICD-10-CM
E11.3512	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye	Diagnosis	ICD-10-CM
E11.3513	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral	Diagnosis	ICD-10-CM
E11.3519	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye	Diagnosis	ICD-10-CM
E11.3521	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E11.3522	right eye Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E11.3523	left eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E11.3529	bilateral Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula,	Diagnosis	ICD-10-CM
E11.3531	unspecified eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E11.3532	macula, right eye Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E11.3533	macula. left eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E11.3539	macula, bilateral Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the	Diagnosis	ICD-10-CM
E11.3541	macula. unspecified eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and	Diagnosis	ICD-10-CM
E11.3542	rhegmatogenous retinal detachment, right eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and	Diagnosis	ICD-10-CM
E11.3543	rhegmatogenous retinal detachment, left eye Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
E11.3549	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal		ICD-10-CM
	detachment and		
	rhegmatogenous retinal detachment, unspecified eve		
E11.3551	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, right eye	Diagnosis	ICD-10-CM
E11.3552	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, left eye	Diagnosis	ICD-10-CM
E11.3553	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	Diagnosis	ICD-10-CM
E11.3559	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye	Diagnosis	ICD-10-CM
E11.3591	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye	Diagnosis	ICD-10-CM
E11.3592	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye	Diagnosis	ICD-10-CM
E11.3593	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral	Diagnosis	ICD-10-CM
E11.3599	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye	Diagnosis	ICD-10-CM
E11.36	Type 2 diabetes mellitus with diabetic cataract	Diagnosis	ICD-10-CM
E11.37X1	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye	Diagnosis	ICD-10-CM
E11.37X2	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye	Diagnosis	ICD-10-CM
E11.37X3	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral	Diagnosis	ICD-10-CM
E11.37X9	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye	Diagnosis	ICD-10-CM
E11.39	Type 2 diabetes mellitus with other diabetic ophthalmic complication	Diagnosis	ICD-10-CM
E11.40	Type 2 diabetes mellitus with diabetic neuropathy, unspecified	Diagnosis	ICD-10-CM
E11.41	Type 2 diabetes mellitus with diabetic mononeuropathy	Diagnosis	ICD-10-CM
E11.42	Type 2 diabetes mellitus with diabetic polyneuropathy	Diagnosis	ICD-10-CM
E11.43	Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy	Diagnosis	ICD-10-CM
E11.44	Type 2 diabetes mellitus with diabetic amyotrophy	Diagnosis	ICD-10-CM
E11.49	Type 2 diabetes mellitus with other diabetic neurological complication	Diagnosis	ICD-10-CM
E11.51	Type 2 diabetes mellitus with diabetic peripheral angiopathy without gangrene	Diagnosis	ICD-10-CM
E11.52	Type 2 diabetes mellitus with diabetic peripheral angiopathy with gangrene	Diagnosis	ICD-10-CM
E11.59	Type 2 diabetes mellitus with other circulatory complications	Diagnosis	ICD-10-CM
E11.610	Type 2 diabetes mellitus with diabetic neuropathic arthropathy	Diagnosis	ICD-10-CM
E11.618	Type 2 diabetes mellitus with other diabetic arthropathy	Diagnosis	ICD-10-CM
E11.620	Type 2 diabetes mellitus with diabetic dermatitis	Diagnosis	ICD-10-CM
E11.621	Type 2 diabetes mellitus with foot ulcer	Diagnosis	ICD-10-CM
E11.622	Type 2 diabetes mellitus with other skin ulcer	Diagnosis	ICD-10-CM
E11.628	Type 2 diabetes mellitus with other skin complications	Diagnosis	ICD-10-CM
E11.630	Type 2 diabetes mellitus with periodontal disease	Diagnosis	ICD-10-CM
E11.638	Type 2 diabetes mellitus with other oral complications	Diagnosis	ICD-10-CM
E11.641	Type 2 diabetes mellitus with hypoglycemia with coma	Diagnosis	ICD-10-CM
E11.649	Type 2 diabetes mellitus with hypoglycemia without coma	Diagnosis	ICD-10-CM
E11.65	Type 2 diabetes mellitus with hyperglycemia	Diagnosis	ICD-10-CM
E11.69	Type 2 diabetes mellitus with other specified complication	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
E11.8	Type 2 diabetes mellitus with unspecified complications	Diagnosis	ICD-10-CM
E11.9	Type 2 diabetes mellitus without complications	Diagnosis	ICD-10-CM
E13.00	Other specified diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-	Diagnosis	ICD-10-CM
	hyperosmolar coma		
	(NKHHC)		
E13.01	Other specified diabetes mellitus with hyperosmolarity with coma	Diagnosis	ICD-10-CM
E13.10	Other specified diabetes mellitus with ketoacidosis without coma	Diagnosis	ICD-10-CM
E13.11	Other specified diabetes mellitus with ketoacidosis with coma	Diagnosis	ICD-10-CM
E13.21	Other specified diabetes mellitus with diabetic nephropathy	Diagnosis	ICD-10-CM
E13.22	Other specified diabetes mellitus with diabetic chronic kidney disease	Diagnosis	ICD-10-CM
E13.29	Other specified diabetes mellitus with other diabetic kidney complication	Diagnosis	ICD-10-CM
E13.311	Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema	Diagnosis	ICD-10-CM
E13.319	Other specified diabetes mellitus with unspecified diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema		
E13.3211	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, right eye		
E13.3212	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, left eye		
E13.3213	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, bilateral		
E13.3219	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, unspecified eye		
E13.3291	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, right eye		
E13.3292	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, left eye		
E13.3293	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, bilateral		
E13.3299	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, unspecified		
540 0044	eve		100 10 011
E13.3311	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
E42 2242	macular edema, right eye	Di	ICD 40 CM
E13.3312	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
E42 2242	macular edema, left eye	Di	ICD 40 CM
E13.3313	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
F12 2210	macular edema, bilateral	Diamoria	ICD 10 CM
E13.3319	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
	macular edema, unspecified		
E12 2201	eye Other specified dishetes mellitus with mederate pennseliferative dishetic retinanethy without	Diagnosis	ICD 10 CM
E13.3391	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, right		
E12 2202	eve Other specified disheres mollitus with moderate penpreliferative disheris retinenathy without	Diagnosia	ICD 10 CM
E13.3392	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, left eye		

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		Code	
Code	Description	Category	Code Type
E13.3393	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E42 2200	macular edema, bilateral	D: :	100 40 614
E13.3399	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, unspecified eye		
E13.3411	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
210.0 .11	macular edema, right eye	Diagnosis	100 10 0111
E13.3412	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
	macular edema, left eye	_	
E13.3413	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
	macular edema, bilateral		
E13.3419	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
	macular edema, unspecified		
E13.3491	eve Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E13.3431	macular edema, right eye	Diagnosis	ICD-10-CIVI
E13.3492	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, left eye	- 10.011211	
E13.3493	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema, bilateral		
E13.3499	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
	macular edema,		
E42 2E44	unspecified eye	5	100 40 614
E13.3511	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E13.3512	right eye Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
L13.3312	left eye	Diagnosis	ICD-10-CIVI
E13.3513	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
	bilateral	J	
E13.3519	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
	unspecified eye		
E13.3521	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment involving the		
E13.3522	macula, right eye	Diamonia	ICD 10 CM
E13.3522	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment involving the macula, left eve		
E13.3523	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment involving the	- 10.011211	
	macula, bilateral		
E13.3529	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment involving the		
	macula, unspecified eve		
E13.3531	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment not involving		
	the macula, right eye		

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		Code	
Code	Description	Category	Code Type
E13.3532	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment not involving		
	the macula, left eve		
E13.3533	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment not involving		
E42 2E20	the macula, bilateral	Diamenia	ICD 10 CM
E13.3539	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment not involving		
E13.3541	the macula. unspecified eve Other specified diabetes mellitus with proliferative diabetic retinopathy with combined	Diagnosis	ICD-10-CM
L13.3341	traction retinal detachment and	Diagnosis	ICD-10-CIVI
	rhegmatogenous retinal detachment, right eve		
E13.3542	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined	Diagnosis	ICD-10-CM
	traction retinal detachment and	- 10011011	
	rhegmatogenous retinal detachment, left eye		
E13.3543	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined	Diagnosis	ICD-10-CM
	traction retinal detachment and	J	
	rhegmatogenous retinal detachment, bilateral		
E13.3549	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined	Diagnosis	ICD-10-CM
	traction retinal detachment and		
	rhegmatogenous retinal detachment, unspecified eye		
E13.3551	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, right eye	Diagnosis	ICD-10-CM
E42 2EE2		Diamonia	ICD 10 CM
E13.3552	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, left eye	Diagnosis	ICD-10-CM
	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	Diagnosis	ICD-10-CM
	other specified diabetes memas with stable promerative diabetic retinopatity, shaterar	Diagnosis	100 10 0141
E13.3553	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, unspecified	Diagnosis	ICD-10-CM
	eye	J	
E13.3559	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, right eye		
E13.3591	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, left eye		
E13.3592	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, bilateral		
E13.3593	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
540.0500	edema, unspecified eye	<u>.</u> .	100 10 011
E13.3599	Other specified diabetes mellitus with diabetic cataract	Diagnosis	ICD-10-CM
E13.36	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment,	Diagnosis	ICD-10-CM
E12 27V1	right eye Other specified diabetes mellitus with diabetic macular edema, resolved following treatment,	Diagnosis	ICD 10 CM
E13.37X1	left eve	Diagnosis	ICD-10-CM
E13.37X2	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment,	Diagnosis	ICD-10-CM
L13.3/ \Z	bilateral	Diagilosis	ICD-TO-CIAI
E13.37X3	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment,	Diagnosis	ICD-10-CM
	unspecified eye		
E13.37X9	Other specified diabetes mellitus with other diabetic ophthalmic complication	Diagnosis	ICD-10-CM
	·	O .	

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		Code	
Code	Description	Category	Code Type
E13.39	Other specified diabetes mellitus with diabetic neuropathy, unspecified	Diagnosis	ICD-10-CM
E13.40	Other specified diabetes mellitus with diabetic mononeuropathy	Diagnosis	ICD-10-CM
E13.41	Other specified diabetes mellitus with diabetic polyneuropathy	Diagnosis	ICD-10-CM
E13.42	Other specified diabetes mellitus with diabetic autonomic (poly)neuropathy	Diagnosis	ICD-10-CM
E13.43	Other specified diabetes mellitus with diabetic amyotrophy	Diagnosis	ICD-10-CM
E13.44	Other specified diabetes mellitus with other diabetic neurological complication	Diagnosis	ICD-10-CM
E13.49	Other specified diabetes mellitus with diabetic peripheral angiopathy without gangrene	Diagnosis	ICD-10-CM
E13.51	Other specified diabetes mellitus with diabetic peripheral angiopathy with gangrene	Diagnosis	ICD-10-CM
E13.52	Other specified diabetes mellitus with other circulatory complications	Diagnosis	ICD-10-CM
E13.59	Other specified diabetes mellitus with diabetic neuropathic arthropathy	Diagnosis	ICD-10-CM
E13.610	Other specified diabetes mellitus with other diabetic arthropathy	Diagnosis	ICD-10-CM
E13.618	Other specified diabetes mellitus with diabetic dermatitis	Diagnosis	ICD-10-CM
E13.620	Other specified diabetes mellitus with foot ulcer	Diagnosis	ICD-10-CM
E13.621	Other specified diabetes mellitus with other skin ulcer	Diagnosis	ICD-10-CM
E13.622	Other specified diabetes mellitus with other skin complications	Diagnosis	ICD-10-CM
E13.628	Other specified diabetes mellitus with periodontal disease	Diagnosis	ICD-10-CM
E13.630	Other specified diabetes mellitus with other oral complications	Diagnosis	ICD-10-CM
E13.638	Other specified diabetes mellitus with hypoglycemia with coma	Diagnosis	ICD-10-CM
E13.641	Other specified diabetes mellitus with hypoglycemia without coma	Diagnosis	ICD-10-CM
E13.649	Other specified diabetes mellitus with hyperglycemia	Diagnosis	ICD-10-CM
E13.65	Other specified diabetes mellitus with other specified complication	Diagnosis	ICD-10-CM
E13.69	Other specified diabetes mellitus with unspecified complications	Diagnosis	ICD-10-CM
E13.8	Other specified diabetes mellitus without complications	Diagnosis	ICD-10-CM
E13.9	Diabetes outpatient self-management training services, individual, per 30 minutes	Procedure	HCPCS
G0108	Diabetes outpatient self-management training services, group session (2 or more), per 30 minutes	Procedure	HCPCS
G0109	Initial physician evaluation and management of a diabetic patient with diabetic sensory	Procedure	HCPCS
	neuropathy resulting in a loss		
	of protective sensation (LOPS) which must include: (1) the diagnosis of LOPS, (2) a patient history, (3) a physical		
C024F	examination tha	Duagadiina	HCDCC
G0245	Follow-up physician evaluation and management of a diabetic patient with diabetic sensory neuropathy resulting in a	Procedure	HCPCS
	loss of protective sensation (LOPS) to include at least the following: (1) a patient history, (2) a		
	physical examination		
G0246	that includes Routine foot care by a physician of a diabetic patient with diabetic sensory neuropathy	Procedure	HCPCS
	resulting in a loss of protective		
	sensation (LOPS) to include the local care of superficial wounds (i.e., superficial to muscle and		
	fascia) and at least		
G0247	the follo Diabetic patient with most recent hemoglobin A1c level (within the last 6 months)	Procedure	HCPCS
	documented as greater than 9%		

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Code	Description	Code Category	Code Type
G8015	Diabetic patient with most recent hemoglobin A1c level (within the last 6 months)	Procedure	
	documented as less than or equal to 9%		
G8016	Clinician documented that diabetic patient was not eligible candidate for hemoglobin A1c measure	Procedure	HCPCS
G8017	Clinician has not provided care for the diabetic patient for the required time for hemoglobin	Procedure	HCPCS
G8018	A1c measure (6 months) Diabetic patient with most recent low-density lipoprotein (within the last 12 months) documented as greater than or	Procedure	HCPCS
G8019	eaual to 100 mg/dl Diabetic patient with most recent low-density lipoprotein (within the last 12 months) documented as less than 100	Procedure	HCPCS
G8020	mg/dl Clinician documented that diabetic patient was not eligible candidate for low-density	Procedure	HCPCS
G8021	lipoprotein measure Clinician has not provided care for the diabetic patient for the required time for low-density lipoprotein measure (12	Procedure	HCPCS
G8022	months) Diabetic patient with most recent blood pressure (within the last 6 months) documented as equal to or greater than	Procedure	HCPCS
G8023	140 systolic or equal to or greater than 80 mm Hg diastolic Diabetic patient with most recent blood pressure (within the last 6 months) documented as less than 140 systolic and	Procedure	HCPCS
G8024	less than 80 diastolic Clinician documented that the diabetic patient was not eligible candidate for blood pressure	Procedure	HCPCS
G8025	measure Clinician has not provided care for the diabetic patient for the required time for blood pressure measure (within the	Procedure	HCPCS
G8026	last 6 months) Clinician has not provided care for the diabetic retinopathy patient for the required time for macular edema and	Procedure	HCPCS
G8332	retinopathy measurement Patient documented to have had findings of macular or fundus exam communicated to the physician managing the	Procedure	HCPCS
G8333	diabetes care Documentation of findings of macular or fundus exam not communicated to the physician managing the patient's	Procedure	HCPCS
G8334	ongoing diabetes care Clinician documentation that patient was not an eligible candidate for the findings of their macular or fundus exam	Procedure	HCPCS
	being communicated to the physician managing their diabetes care during the reporting year		
G8335	Clinician has not provided care for the diabetic retinopathy patient for the required time for physician communication measurement	Procedure	HCPCS
G8336	Diabetic patients with no documentation of hemoglobin A1c level (within the last 12 months)	Procedure	HCPCS

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Code	Description	Code Category	Code Type
G8385	Diabetic patients with no documentation of low-density lipoprotein (within the last 12	Procedure	HCPCS
	months)		
G8386	Diabetic patients with no documentation of blood pressure measurement (within the last 12	Procedure	HCPCS
	months)		
	Ischemic Heart Disease		
411	Other acute and subacute forms of ischemic heart disease	Diagnosis	ICD-9-CM
411.0	Postmyocardial infarction syndrome	Diagnosis	ICD-9-CM
411.1	Intermediate coronary syndrome	Diagnosis	ICD-9-CM
411.8	Other acute and subacute forms of ischemic heart disease	Diagnosis	ICD-9-CM
411.81	Acute coronary occlusion without myocardial infarction	Diagnosis	ICD-9-CM
411.89	Other acute and subacute form of ischemic heart disease	Diagnosis	ICD-9-CM
413	Angina pectoris	Diagnosis	ICD-9-CM
413.0	Angina decubitus	Diagnosis	ICD-9-CM
413.1	Prinzmetal angina	Diagnosis	ICD-9-CM
413.9	Other and unspecified angina pectoris	Diagnosis	ICD-9-CM
414	Other forms of chronic ischemic heart disease	Diagnosis	ICD-9-CM
414.0	Coronary atherosclerosis	Diagnosis	ICD-9-CM
414.00	Coronary atherosclerosis of unspecified type of vessel, native or graft	Diagnosis	ICD-9-CM
414.01	Coronary atherosclerosis of native coronary artery	Diagnosis	ICD-9-CM
414.02	Coronary atherosclerosis of autologous vein bypass graft	Diagnosis	ICD-9-CM
414.03	Coronary atherosclerosis of nonautologous biological bypass graft	Diagnosis	ICD-9-CM
414.04	Coronary atherosclerosis of artery bypass graft	Diagnosis	ICD-9-CM
414.05	Coronary atherosclerosis of unspecified type of bypass graft	Diagnosis	ICD-9-CM
414.06	Coronary atherosclerosis, of native coronary artery of transplanted heart	Diagnosis	ICD-9-CM
414.07	Coronary atherosclerosis, of bypass graft (artery) (vein) of transplanted heart	Diagnosis	ICD-9-CM
414.1	Aneurysm and dissection of heart	Diagnosis	ICD-9-CM
414.10	Aneurysm of heart	Diagnosis	ICD-9-CM
414.11	Aneurysm of coronary vessels	Diagnosis	ICD-9-CM
414.12	Dissection of coronary artery	Diagnosis	ICD-9-CM
414.19	Other aneurysm of heart	Diagnosis	ICD-9-CM
414.2	Chronic total occlusion of coronary artery	Diagnosis	ICD-9-CM
414.3	Coronary atherosclerosis due to lipid rich plaque	Diagnosis	ICD-9-CM
414.4	Coronary atherosclerosis due to ripid her plaque	Diagnosis	ICD-9-CM
414.8	Other specified forms of chronic ischemic heart disease	Diagnosis	ICD-9-CIVI
414.9	Unspecified chronic ischemic heart disease	_	ICD-9-CM
429.2	Unspecified cardiovascular disease	Diagnosis Diagnosis	ICD-9-CM
429.5	Rupture of chordae tendineae	Diagnosis	ICD-9-CM
	·	_	
429.6	Rupture of papillary muscle	Diagnosis	ICD-9-CM
429.7	Certain sequelae of myocardial infarction, not elsewhere classified	Diagnosis	ICD-9-CM
429.71	Acquired cardiac septal defect Other certain seguelae of myospadial inferstion, not elsewhere classified	Diagnosis	ICD-9-CM
429.79	Other certain sequelae of myocardial infarction, not elsewhere classified	Diagnosis	ICD-9-CM
429.9	Unspecified heart disease	Diagnosis	ICD-9-CM
G8033	Prior myocardial infarction, coronary artery disease patient documented to be on beta-blocker	Procedure	HCPCS
G8034	therapy Prior myocardial infarction, coronary artery disease patient not documented to be on beta-	Procedure	HCPCS
	blocker therapy		

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		Code	
Code	Description	Category	Code Type
G8035	Clinician documented that prior myocardial infarction, coronary artery disease patient was not	Procedure	HCPCS
	eligible candidate for		
G8036	beta-blocker therapy measure Coronary artery disease patient documented to be on antiplatelet therapy	Procedure	HCPCS
G8037	Coronary artery disease patient documented to be on antiplatelet therapy	Procedure	HCPCS
G8038	Clinician documented that coronary artery disease patient was not eligible candidate for	Procedure	HCPCS
00030	antiplatelet therapy measure	rroccaure	rici es
G8039	Coronary artery disease patient with low-density lipoprotein documented to be greater than	Procedure	HCPCS
00033	100 mg/dl	rroccaare	1101 05
G8040	Coronary artery disease patient with low-density lipoprotein documented to be less than or	Procedure	HCPCS
000.0	equal to 100 mg/dl		
G8041	Clinician documented that coronary artery disease patient was not eligible candidate for low-	Procedure	HCPCS
	density lipoprotein		
	measure		
120.0	Unstable angina	Diagnosis	ICD-10-CM
120.1	Angina pectoris with documented spasm	Diagnosis	ICD-10-CM
120.8	Other forms of angina pectoris	Diagnosis	ICD-10-CM
120.9	Angina pectoris, unspecified	Diagnosis	ICD-10-CM
123.0	Hemopericardium as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.1	Atrial septal defect as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.2	Ventricular septal defect as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.3	Rupture of cardiac wall without hemopericardium as current complication following acute	Diagnosis	ICD-10-CM
	myocardial infarction		
123.4	Rupture of chordae tendineae as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.5	Rupture of papillary muscle as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.6	Thrombosis of atrium, auricular appendage, and ventricle as current complications following	Diagnosis	ICD-10-CM
	acute myocardial		
	infarction		
123.7	Postinfarction angina	Diagnosis	ICD-10-CM
123.8	Other current complications following acute myocardial infarction	Diagnosis	ICD-10-CM
124.0	Acute coronary thrombosis not resulting in myocardial infarction	Diagnosis	ICD-10-CM
124.1	Dressler's syndrome	Diagnosis	ICD-10-CM
124.8	Other forms of acute ischemic heart disease	Diagnosis	ICD-10-CM
124.9	Acute ischemic heart disease, unspecified	Diagnosis	ICD-10-CM
125.10	Atherosclerotic heart disease of native coronary artery without angina pectoris	Diagnosis	ICD-10-CM
125.110	Atherosclerotic heart disease of native coronary artery with unstable angina pectoris	Diagnosis	ICD-10-CM
125.111	Atherosclerotic heart disease of native coronary artery with angina pectoris with documented	Diagnosis	ICD-10-CM
125.118	spasm Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris	Diagnosis	ICD-10-CM
123.110	Atheroscierotic heart disease of hative coronary aftery with other forms of angina pectoris	Diagnosis	ICD-TO-CIAI
125.119	Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris	Diagnosis	ICD-10-CM
125.3	Aneurysm of heart	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
125.41	Coronary artery aneurysm	Diagnosis	ICD-10-CM
125.42	Coronary artery dissection	Diagnosis	ICD-10-CM
125.5	Ischemic cardiomyopathy	Diagnosis	ICD-10-CM
125.6	Silent myocardial ischemia	Diagnosis	ICD-10-CM
125.700	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris	Diagnosis	ICD-10-CM
125.701	Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm	Diagnosis	ICD-10-CM
125.708	Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris	Diagnosis	ICD-10-CM
125.709	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris	Diagnosis	ICD-10-CM
125.710	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris	Diagnosis	ICD-10-CM
125.711	Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm	Diagnosis	ICD-10-CM
125.718	Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris	Diagnosis	ICD-10-CM
125.719	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris	Diagnosis	ICD-10-CM
125.720	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris	Diagnosis	ICD-10-CM
125.721	Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm	Diagnosis	ICD-10-CM
125.728	Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris	Diagnosis	ICD-10-CM
125.729	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris	Diagnosis	ICD-10-CM
125.730	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable	Diagnosis	ICD-10-CM
125.731	angina pectoris Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented	Diagnosis	ICD-10-CM
125.738	spasm Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms	Diagnosis	ICD-10-CM
125.739	of angina pectoris Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified	Diagnosis	ICD-10-CM
125.750	angina pectoris Atherosclerosis of native coronary artery of transplanted heart with unstable angina	Diagnosis	ICD-10-CM
125.751	Atherosclerosis of native coronary artery of transplanted heart with angina pectoris with documented spasm	Diagnosis	ICD-10-CM
125.758	Atherosclerosis of native coronary artery of transplanted heart with other forms of angina pectoris	Diagnosis	ICD-10-CM
125.759	Atherosclerosis of native coronary artery of transplanted heart with unspecified angina pectoris	Diagnosis	ICD-10-CM
125.760	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina	Diagnosis	ICD-10-CM

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Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina pectoris With documented spasm 125.768 Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of Diagnosis ICD-angina pectoris 125.769 Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified Diagnosis ICD-angina pectoris 125.790 Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris Diagnosis ICD- 125.791 Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD-spasm	2 Type 10-CM 10-CM 10-CM 10-CM
with documented spasm Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of Diagnosis ICD- angina pectoris Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified Diagnosis ICD- angina pectoris Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris Diagnosis ICD- 125.791 Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD- spasm	10-CM 10-CM 10-CM
Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris 125.769 Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified Diagnosis ICD-angina pectoris 125.790 Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris 125.791 Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD-spasm	10-CM 10-CM
angina pectoris Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified Diagnosis ICD- angina pectoris Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris Diagnosis ICD- Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD- spasm	10-CM 10-CM
Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified Diagnosis ICD- angina pectoris 125.790 Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris Diagnosis ICD- 125.791 Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD- spasm	10-CM
angina pectoris Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris Diagnosis ICD- Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD- spasm	10-CM
Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris Diagnosis ICD- Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD- spasm	
I25.791 Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented Diagnosis ICD-spasm	
spasm	10-CM
spasm	10-CIVI
·	
125.798 Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris Diagnosis ICD-	10-CM
Atherosciciosis of other coronary artery bypass grant(s) with other forms of alignia pectoris — blaghosis—feb	TO CIVI
125.799 Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris Diagnosis ICD-	10-CM
, , , , , , , , , , , , , , , , , , , ,	10-CM
Atherosclerosis of native coronary artery of transplanted heart without angina pectoris Diagnosis ICD-	10-CM
125 042 Akkanan kanan kanan kanan merina di kanan	40 CN4
	10-CM
pectoris 125.82 Chronic total occlusion of coronary artery Diagnosis ICD-	10-CM
, ,	10-CIVI
· · · · · · · · · · · · · · · · · · ·	10-CIVI
, ,	10-CIVI
	10-CIVI
· ·	10-CIVI
·	10-CM
	10-CM
· · · · · · · · · · · · · · · · · · ·	10-CM
	10-CM
Renal Disorders	TO CIVI
	-9-CM
584.5 Acute kidney failure with lesion of tubular necrosis Diagnosis ICD	-9-CM
584.6 Acute kidney failure with lesion of renal cortical necrosis Diagnosis ICD-	-9-CM
584.7 Acute kidney failure with lesion of medullary [papillary] necrosis Diagnosis ICD-	-9-CM
584.8 Acute kidney failure with other specified pathological lesion in kidney Diagnosis ICD-	-9-CM
584.9 Acute kidney failure, unspecified Diagnosis ICD-	-9-CM
585 Chronic kidney disease (CKD) Diagnosis ICD-	-9-CM
585.1 Chronic kidney disease, Stage I Diagnosis ICD-	-9-CM
585.2 Chronic kidney disease, Stage II (mild) Diagnosis ICD-	-9-CM
585.3 Chronic kidney disease, Stage III (moderate) Diagnosis ICD-	-9-CM
585.4 Chronic kidney disease, Stage IV (severe) Diagnosis ICD	-9-CM
585.5 Chronic kidney disease, Stage V Diagnosis ICD-	-9-CM
585.6 End stage renal disease Diagnosis ICD-	-9-CM
585.9 Chronic kidney disease, unspecified Diagnosis ICD-	-9-CM
586 Unspecified renal failure Diagnosis ICD-	-9-CM
	-9-CM
N17.0 Acute kidney failure with tubular necrosis Diagnosis ICD-	10-CM

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		Code	
Code	Description	Category	Code Type
N17.1	Acute kidney failure with acute cortical necrosis	Diagnosis	ICD-10-CM
N17.2	Acute kidney failure with medullary necrosis	Diagnosis	ICD-10-CM
N17.8	Other acute kidney failure	Diagnosis	ICD-10-CM
N17.9	Acute kidney failure, unspecified	Diagnosis	ICD-10-CM
N18.1	Chronic kidney disease, stage 1	Diagnosis	ICD-10-CM
N18.2	Chronic kidney disease, stage 2 (mild)	Diagnosis	ICD-10-CM
N18.3	Chronic kidney disease, stage 3 (moderate)	Diagnosis	ICD-10-CM
N18.4	Chronic kidney disease, stage 4 (severe)	Diagnosis	ICD-10-CM
N18.5	Chronic kidney disease, stage 5	Diagnosis	ICD-10-CM
N18.6	End stage renal disease	Diagnosis	ICD-10-CM
N18.9	Chronic kidney disease, unspecified	Diagnosis	ICD-10-CM
N19	Unspecified kidney failure	Diagnosis	ICD-10-CM
N26.1	Atrophy of kidney (terminal)	Diagnosis	ICD-10-CM
N26.9	Renal sclerosis, unspecified	Diagnosis	ICD-10-CM

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Brand Name Generic Name Allergy Treatments Chlorpheniramine Maleate/Codeine Cotabflu Phosphate/Acetaminophen DIPHENHYDRAMINE HCL Dicopanol acetaminophen/dextromethorphan HBr Child Cough and Sore Throat Tudorza Pressair aclidinium bromide albuterol sulfate ProAir HFA albuterol sulfate ProAir RespiClick albuterol sulfate Proventil HFA albuterol sulfate Ventolin HFA albuterol sulfate Vospire ER albuterol sulfate albuterol sulfate alcaftadine Lastacaft aldosterone aldosterone (bulk) aminophylline aminophylline aminophylline aminophylline (bulk) arformoterol tartrate Brovana azelastine HCl Astelin azelastine HCl Astepro azelastine HCl Optivar azelastine HCl azelastine azelastine HCl/fluticasone propionate Dymista azelastine/fluticasone/sodium chloride/sodium **Ticalast** bicarbonate beclomethasone dipropionate Beconase AQ beclomethasone dipropionate **QNASL** beclomethasone dipropionate Qvar **Qvar RediHaler** beclomethasone dipropionate benralizumab Fasenra bepotastine besilate **Bepreve** betamethasone acetate and sodium phos in sterile betameth ac, sodphos(PF)-water water/PF betamethasone acetate and sodium **Betaloan SUIK** phosph/norflurane/HFC 245fa Pod-Care 100CG betamethasone acetate and sodium phosph/norflurane/HFC 245fa betamethasone acetate/betamethasone sodium Beta-1 phosphate betamethasone acetate/betamethasone sodium Celestone Soluspan phosphate betamethasone acetate/betamethasone sodium Pod-Care 100C phosphate betamethasone acetate/betamethasone sodium ReadySharp Betamethasone phosphate betamethasone acetate/betamethasone sodium betamethasone acet, sod phos phosphate betamethasone acetate/betamethasone sodium betamethasone ace, sodphos-wtr phosphate/water betamethasone sodium phosph in sterile water for betamethasone sodphosph-water injection

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J-TAN PD

brompheniramine maleate



Generic Name	Brand Name
brompheniramine maleate	brompheniramine maleate(bulk)
brompheniramine maleate/phenylephrine HCl	Children's Cold-Allergy (PE)
brompheniramine maleate/phenylephrine HCl	Dimaphen (PE)
brompheniramine maleate/phenylephrine HCl	Glenmax PEB
brompheniramine maleate/phenylephrine HCl	Relhist BP
brompheniramine maleate/phenylephrine	Trexbrom
HCI/chlophedianol HCI	TEXOTOTI
brompheniramine maleate/phenylephrine	M-END PE
HCI/codeine phosphate	
brompheniramine maleate/phenylephrine	Poly-Tussin AC
HCI/codeine phosphate	
brompheniramine maleate/phenylephrine	AP-Hist DM
HCI/dextromethorphan	711 11130 5141
brompheniramine maleate/phenylephrine	Ala-Hist DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Altipres-B
HCI/dextromethorphan	, p. 65 2
brompheniramine maleate/phenylephrine	Bio T Pres-B
HCI/dextromethorphan	3.0 1 1 1 30 2
brompheniramine maleate/phenylephrine	BroveX PEB DM
HCI/dextromethorphan	5.0.0
brompheniramine maleate/phenylephrine	Children's Cold and Cough(PE)
HCI/dextromethorphan	omaren s cola ana coasilir 27
brompheniramine maleate/phenylephrine	Children's Cold and CoughDM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Children's Dibromm DMCold-Cou
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Cold and Cough DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Cold and Cough Elixir
HCI/dextromethorphan	ŭ
brompheniramine maleate/phenylephrine	Dimaphen DM
HCI/dextromethorphan	·
brompheniramine maleate/phenylephrine	Dimetapp DM Cold-Cough(PE)
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	EndaCof - DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Glenmax PEB DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Glenmax PEB DM Forte
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	LoHist PEB DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	LoHist-DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	M-Hist DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Niva-Hist DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Presgen B
HCI/dextromethorphan	

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Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request

Generic Name	Brand Name
brompheniramine maleate/phenylephrine	RelCof DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Rynex DM
HCI/dextromethorphan	, -
brompheniramine maleate/phenylephrine	Tussi Pres-B
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	Wal-tap DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine	brompheniramin-phenylephrin-DM
HCI/dextromethorphan	F - 7 - F
brompheniramine maleate/pseudoephedrine	Atuss DA
HCI/chlophedianol	
brompheniramine maleate/pseudoephedrine	brompheniramine-pseudoeph-DM
HCI/dextromethorphan	Stomphomatime produceph 2111
budesonide	Pulmicort
budesonide	Pulmicort Flexhaler
budesonide	Rhinocort Allergy
budesonide	Rhinocort Aqua
budesonide	budesonide
budesonide, micronized	budesonide, micronized (bulk)
budesonide/formoterol fumarate	Symbicort
carbinoxamine maleate	Arbinoxa
carbinoxamine maleate	Karbinal ER
carbinoxamine maleate	PALGIC
carbinoxamine maleate	RyVent
carbinoxamine maleate	carbinoxamine maleate
cetirizine HCl	24Hour Allergy
cetirizine HCl	All Day Allergy (cetirizine)
cetirizine HCl	All Day Allergy Relief(cetir)
cetirizine HCl	Aller-Tec
cetirizine HCl	Allergy Relief (cetirizine)
cetirizine HCl	Child Allergy Relf(cetirizine)
cetirizine HCl	Child's All Day Allergy(cetir)
cetirizine HCl	Children's Aller-Tec
cetirizine HCl	Children's Allergy Complete
cetirizine HCl	Children's Allergy Complete Children's Allergy (cetirizine)
cetirizine HCl	Children's Cetirizine
cetirizine HCl	Children's Wal-Zyr
cetirizine HCl	Children's Wai-Zyi Children's Zyrtec Allergy
cetirizine HCl	Wal-Zyr (cetirizine)
cetirizine HCl	Zyrtec
cetirizine HCl	cetirizine
	All Day Allergy-D
cetirizine HCI/pseudoephedrine HCI	Aller-Tec D
cetirizine HCl/pseudoephedrine HCl cetirizine HCl/pseudoephedrine HCl	
·	Allergy Complete-D
cetirizine HCl/pseudoephedrine HCl	Allergy D-12
cetirizine HCl/pseudoephedrine HCl	Allergy Relief-D (cetirizine)
cetirizine HCI/pseudoephedrine HCI	Allergy-Congest Relief-D (cet)
cetirizine HCI/pseudoephedrine HCI	Cetiri-D
cetirizine HCl/pseudoephedrine HCl	Wal-Zyr D
cetirizine HCl/pseudoephedrine HCl	Zyrtec-D

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Generic Name	Brand Name
cetirizine HCI/pseudoephedrine HCI	cetirizine-pseudoephedrine
chlophedianol HCl/guaifenesin	Chlo Tuss EX
chlophedianol HCl/guaifenesin	Vanacof G
chlophedianol HCl/guaifenesin	chlophedianol-guaifenesin
chlorcyclizine HCl	Ahist (chlorcyclizine)
chlorcyclizine HCI/codeine phosphate	Poly-Tussin
chlorcyclizine HCl/phenylephrine HCl	Dallergy (chlorcyclizine-PE)
chlorcyclizine HCl/pseudoephedrine HCl	Nasopen
chlorcyclizine HCl/pseudoephedrine HCl	Stahist AD
chlorcyclizine HCl/pseudoephedrine	Biclora-D
HCI/chlophedianol HCI	5.0.0.0 2
chlorcyclizine HCl/pseudoephedrine HCl/codeine	Poly-Tussin D
phosphate	. 0.,
chlorcyclizine hydrochloride/chlophedianol	Biclora
hydrochloride	Sidiord
chlorpheniram/phenyleph/dextromethorphn	Cold-Flu M-SymptomDay-Night
/acetaminophen/guaifn	cold that it symptomout this it
chlorpheniram/phenyleph/dextromethorphn	Tylenol Cold-Flu SevereDay-Nt
/acetaminophen/guaifn	Tylenor cold the severebay ive
chlorpheniramine maleate	Aller-Chlor
chlorpheniramine maleate	Allergy (chlorpheniramine)
chlorpheniramine maleate	Allergy 4-Hour
chlorpheniramine maleate	Allergy Relief(chlorpheniramn)
chlorpheniramine maleate	Allergy-Time
chlorpheniramine maleate	Chlor-Trimeton
chlorpheniramine maleate	Chlorphen SR
chlorpheniramine maleate	ED Chlorped Jr
chlorpheniramine maleate	Ed-ChlorPed
chlorpheniramine maleate	Ed-Chlortan
chlorpheniramine maleate	Pharbechlor
chlorpheniramine maleate	Wal-Finate
chlorpheniramine maleate	chlorpheniramine maleate
chlorpheniramine maleate/codeine phosphate	Codar AR
chlorpheniramine maleate/codeine phosphate	EndaCof-C
chlorpheniramine maleate/codeine phosphate	Tuxarin ER
chlorpheniramine maleate/codeine phosphate	Z-Tuss AC
chlorpheniramine maleate/codeine phosphate	Zodryl AC 25
chlorpheniramine maleate/codeine phosphate	Zodryl AC 30
chlorpheniramine maleate/codeine phosphate	Zodryl AC 35
chlorpheniramine maleate/codeine phosphate	Zodryl AC 40
chlorpheniramine maleate/codeine phosphate	Zodryl AC 50
chlorpheniramine maleate/codeine phosphate	Zodryl AC 60
chlorpheniramine maleate/codeine phosphate	Zodryl AC 80
chlorpheniramine maleate/dextromethorphan HBr	Chld Robitussin Night CoughDM
chlorpheniramine maleate/dextromethorphan HBr	Cough and Cold(chlorphen-DM)
chlorpheniramine maleate/dextromethorphan HBr	Cough-Cold Relief HBP
chlorpheniramine maleate/dextromethorphan HBr	Maxi-TussDM(chlorpheniramine)
chlorpheniramine maleate/dextromethorphan HBr	Scot-Tussin DM
chlorpheniramine maleate/phenylephrine HCl	Cold and Allergy
chlorpheniramine maleate/phenylephrine HCl	Sinus and Allergy PE
chlorpheniramine maleate/phenylephrine HCl	Sinus-Allergy (phenylephrine)
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Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request

Generic Name	Brand Name
chlorpheniramine maleate/phenylephrine	Carbaphen CH
HCI/chlophedianol HCI	•
chlorpheniramine maleate/phenylephrine	Carbaphen Ped CH
HCI/chlophedianol HCl	·
chlorpheniramine maleate/phenylephrine	ExaPhen CH
HCI/chlophedianol HCI	
chlorpheniramine maleate/phenylephrine	Phenagil CH
HCI/chlophedianol HCI	
chlorpheniramine maleate/phenylephrine	CapCof
HCI/codeine phosphate	
chlorpheniramine maleate/phenylephrine	Maxi-Tuss CD
HCI/codeine phosphate	
chlorpheniramine maleate/phenylephrine	Bio-Rytuss
HCI/dextromethorphan	
chlorpheniramine maleate/phenylephrine	Maxichlor PEH DM
HCI/dextromethorphan	
chlorpheniramine maleate/phenylephrine	Advil Allergy-Congestion RIf
HCI/ibuprofen	
chlorpheniramine maleate/phenylephrine	Cold Relief
bitartrate/aspirin	
chlorpheniramine maleate/phenylephrine	Cold Relief Plus
bitartrate/aspirin	
chlorpheniramine maleate/pseudoephedrine	Tricode AR
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 25
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 30
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 35
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 40
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 50
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 60
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 80
HCI/codeine	
chlorpheniramine maleate/pseudoephedrine	Advil Allergy Sinus
HCI/ibuprofen	
ciclesonide	Alvesco
ciclesonide	Omnaris
ciclesonide	Zetonna
clemastine fumarate	Allergy Relief (clemastine)
clemastine fumarate	Allerhist (clemastine)
clemastine fumarate	Allerhist-1
clemastine fumarate	Dayhist Allergy
clemastine fumarate	Tavist-1
clemastine fumarate	clemastine
clemizole HCl	clemizole HCI (bulk)
codeine phosphate/guaifenesin	G Tussin AC

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Generic Name codeine phosphate/guaifenesin codeine polistriex/chlorpheniramine polistriex cortisone cortisone acteate cortisone cortiso	Canaria Nama	Prond Name
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Generic Name	Brand Name
lexbrompheniramine maleate/phenylephrine HCl	Dallergy(dexbrompheniramn-PE)
lexbrompheniramine maleate/phenylephrine HCl	dexbrompheniramine-phenyleph
exbrompheniramine maleate/pseudoephedrine	Acticon (dexbromph-pse)
ICI	
exbrompheniramine maleate/pseudoephedrine	M-End Max D
ICI/codeine phos	
exchlorpheniramine maleate	Ryclora
exchlorpheniramine maleate	dexchlorpheniramine maleate
exchlorpheniramine maleate/phenylephrine HCl	Rymed(dexchlorpheniramine-PE)
exchlorpheniramine maleate/phenylephrine HCl	Stahist (dexchlorpheniramine)
exchlorpheniramine maleate/phenylephrine	Pro-Red AC (w/dexchlorphenir)
ICI/codeine	
exchlorpheniramine	Polytussin DM
naleate/phenylephrine/dextromethorphan	
extromethorphan	Child Plus Cough andRunnyNose
Br/acetaminophen/chlorpheniramine maleate	· ·
extromethorphan	Child's TylenolplusCough,RNos
Br/acetaminophen/chlorpheniramine maleate	, , , , , , , , , , , , , , , , , , , ,
extromethorphan	Coricidin HBP Flu
Br/acetaminophen/chlorpheniramine maleate	
extromethorphan	Flu BP
Br/acetaminophen/chlorpheniramine maleate	110 51
extromethorphan	Flu HBP
Br/acetaminophen/chlorpheniramine maleate	110 1151
extromethorphan	Maximum Strength Flu
Br/acetaminophen/chlorpheniramine maleate	Waximum Strength Fla
extromethorphan	Vicks NyQuil Cold/Flu (cpm)
IBr/acetaminophen/chlorpheniramine maleate	vicks wy dan coldy na (cpm)
extromethorphan	Diabetic Tussin Night Time
Br/acetaminophen/diphenhydramine HCl	Diabetic russiii Nigrit Time
extromethorphan	All-Nite Cold-Flu
	All-Nite Cold-Flu
lBr/acetaminophen/doxylamine extromethorphan	Cold-Flu Relief
•	Cold-Flu Kellel
IBr/acetaminophen/doxylamine	Contac Cold Fly Night
extromethorphan	Contac Cold-Flu Night
IBr/acetaminophen/doxylamine	Controlling LIDD Collab MarthiConstant
extromethorphan	Coricidin HBP Cold-MultiSympt
Br/acetaminophen/doxylamine	
extromethorphan	Cough-Sore Throat Night
IBr/acetaminophen/doxylamine	
extromethorphan	Night Time
Br/acetaminophen/doxylamine	
extromethorphan	Night Time Cold
Br/acetaminophen/doxylamine	
extromethorphan	Night Time Cold and FluRelief
Br/acetaminophen/doxylamine	
extromethorphan	Night Time Cold-Flu
Br/acetaminophen/doxylamine	
extromethorphan	Night Time Cold-Flu Relief
Br/acetaminophen/doxylamine	

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Generic Name	Brand Name
dextromethorphan	Nighttime Cold-Flu
HBr/acetaminophen/doxylamine	11.6.11.11.10 55.5 11.0
dextromethorphan	Nighttime Cold-Flu Relief
HBr/acetaminophen/doxylamine	
dextromethorphan	Nite Time Cold-Flu
HBr/acetaminophen/doxylamine	Title Time Gold Tid
dextromethorphan	Nite Time Cold-Flu Relief
HBr/acetaminophen/doxylamine	Title Time cold the Relief
dextromethorphan	Nite-Time Cold-Flu
HBr/acetaminophen/doxylamine	Wite Time Cold Tid
dextromethorphan	Nitetime Multi-Symptom
HBr/acetaminophen/doxylamine	Witetime Waiti Symptom
dextromethorphan	Robitussin Cold-Flu Night
HBr/acetaminophen/doxylamine	Nobitussiii Colu Tiu Nigiti
dextromethorphan	Vicks Nature Fusion Cold-Flu
•	VICKS Nature rusion Colu-ru
HBr/acetaminophen/doxylamine dextromethorphan	Vicks NyQuil Cold/FluLiquicap
•	vicks nyquii coiu/FiuLiquicap
HBr/acetaminophen/doxylamine	Viola Nyavil Nighttima Daliaf
dextromethorphan	Vicks Nyquil Nighttime Relief
HBr/acetaminophen/doxylamine	Destine Niehtline Couch
dextromethorphan HBr/doxylamine succinate	Daytime-Nighttime Cough
dextromethorphan HBr/doxylamine succinate	NightTime Cough
dextromethorphan HBr/doxylamine succinate	Nite Time Cough
dextromethorphan HBr/doxylamine succinate	Nitetime Cough
dextromethorphan HBr/doxylamine succinate	Robitussin Nighttime CoughDM
dextromethorphan HBr/doxylamine succinate	SafeTussin PM
dextromethorphan HBr/doxylamine succinate	Tussin Nighttime Cough DM
dextromethorphan HBr/doxylamine succinate	Vicks NyQuil Cough
dextromethorphan HBr/phenylephrine HCl	Children's Cold-CoughDaytime
dextromethorphan HBr/phenylephrine HCl	Children's Sudafed PE Cough
dextromethorphan HBr/phenylephrine HCl	Cold and Cough (pe-dm)
dextromethorphan HBr/phenylephrine HCl	Triaminic Cold and Cough(PE)
dextromethorphan HBr/phenylephrine	Cold Head CongestionDaytime
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Cold Multi-Symptom
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Cold-Flu Relief
HCl/acetaminophen	
dextromethorphan HBr/phenylephrine	Day Multi-Symp Flu-SevereCold
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Day Time PE
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	DayTime
HCl/acetaminophen	
dextromethorphan HBr/phenylephrine	Daytime Cold
HCI/acetaminophen	•
dextromethorphan HBr/phenylephrine	Daytime Cold-Flu
HCl/acetaminophen	,
dextromethorphan HBr/phenylephrine	Daytime Cold-Flu Relief (PE)
HCI/acetaminophen	· / · · · · · · · · · · · · · · · · · ·
Troy accommodition	

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Generic Name	Brand Name
dextromethorphan HBr/phenylephrine	Flu Relief Therapy Daytime
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Flu-Severe Cold-CoughDaytime
HCl/acetaminophen	
dextromethorphan HBr/phenylephrine	HerbioMed Body Aches-SinusM-S
HCI/acetaminophen	, -
dextromethorphan HBr/phenylephrine	Mapap Cold Formula
HCI/acetaminophen	The first of the f
dextromethorphan HBr/phenylephrine	Mucinex Fast-MaxCongest-Head
HCI/acetaminophen	Ç
dextromethorphan HBr/phenylephrine	Mucinex Fast-MaxSevCold-Sinus
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Robitussin Cold-Flu Day
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Sudafed PEPressure-Pain-Cough
HCl/acetaminophen	
dextromethorphan HBr/phenylephrine	Theraflu ExpressMax ColdDay
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Theraflu Multi-Symptom Cold
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Tylenol Cold Max Day
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Tylenol Cold Multi-SymptomDay
HCl/acetaminophen	
dextromethorphan HBr/phenylephrine	Vicks DayQuil Cold-Flu Relief
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Vicks Nature Fusion
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Wal-Flu Severe Cold-Cough
HCI/acetaminophen	
dextromethorphan HBr/phenylephrine	Alahist CF
HCI/dexbrompheniramine	
dextromethorphan HBr/phenylephrine	Alahist DM
HCI/dexbrompheniramine	Dispature DVD
dextromethorphan HBr/phenylephrine	Bionatuss DXP
HCI/dexbrompheniramine	C. D. Tura DVD
dextromethorphan HBr/phenylephrine	G-P-Tuss DXP
HCI/dexbrompheniramine	Supress A
dextromethorphan HBr/phenylephrine	Supress A
HCI/dexbrompheniramine	Alka Saltzar DiurSin Alla Cah
dextromethorphan	Alka-Seltzer PlusSin-Allg-Cgh
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Cold Multi-SymptomNightTime
·	Cola Mala-Symptominight inne
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Cold and Flu Relief Plus (D/N)
	כסום מווע ו וע וזכווכו רועג (ש/ וע)
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Cold-Flu Relief, Day/Night
HBr/phenylephrine/acetaminophen/doxylamine	Colu-i la Nellei, Day/Nigill
dextromethorphan	Daytime-Nighttime
HBr/phenylephrine/acetaminophen/doxylamine	Sayane ingricine
ribit phenylephiniet acetanimophent uoxylanime	

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Generic Name	Brand Name
dextromethorphan	Daytime-Nighttime Cold-Flu
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Mucinex Fast-Max Nite (doxyl)
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Nite Time Cold-Flu Relief (PE)
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Severe Cold and FluNighttime
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Severe Sinus CongestAlrgy-Cgh
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine	Tylenol Cold Max Night
dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine	Tylenol Cold Multi-SymptNight
dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine	Vicks NyQuil Severe Cold-Flu
dextromethorphan HBr/pseudoephedrine HCl/acetaminophen	DAY-TIME
dextromethorphan HBr/pseudoephedrine HCl/acetaminophen	Daytime Cold and Flu Relief
dextromethorphan/phenylephrine/acetaminophen/diphenhydramine	HerbioMed Deep Cold-FluNight
dextromethorphan/phenylephrine/acetaminophen/diphenhydramine	Multi-Symptom SevereCold-Nt
dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine	Alka-Seltzer Plus Cold+Flu
dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine	Night Time Cold Medicine
dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine	Night Time Cold The Balliof
dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine dextromethorphan/pseudoephrine	Night Time Cold-Flu Relief Nite Time
HCI/acetaminophen/doxylamine diclofenac sodium	diclofenac sodium
diphenhydramine HCl	Alka-Seltzer Plus Allergy
diphenhydramine HCl diphenhydramine HCl	Aller-G-Time Allergy
diphenhydramine HCl diphenhydramine HCl	Allergy (diphenhydramine) Allergy Medication
diphenhydramine HCl	Allergy Medicine
diphenhydramine HCl	AllergyRelief(diphenhydramin)
diphenhydramine HCl diphenhydramine HCl	Banophen Banophen Allergy
diphenhydramine HCl	Benadryl
diphenhydramine HCl	Benadryl Allergy
diphenhydramine HCl	Child Allergy Relief (diphen)
diphenhydramine HCl	Children's Allergy (diphenhyd)
diphenhydramine HCl	Children's Allergy Medicine
diphenhydramine HCl diphenhydramine HCl	Children's Benadryl Allergy Children's Diphenhydramine

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Generic Name	Brand Name
diphenhydramine HCl	Children's Wal-Dryl Allergy
diphenhydramine HCl	Complete Allergy
diphenhydramine HCl	Complete Allergy Medicine
diphenhydramine HCl	Compoz
diphenhydramine HCl	Diphedryl
diphenhydramine HCl	Diphen
diphenhydramine HCl	Diphenhist
diphenhydramine HCl	EZ Nite Sleep
diphenhydramine HCl	Geri-Dryl
diphenhydramine HCl	Medi-Phedryl
diphenhydramine HCl	Naramin
diphenhydramine HCl	NightTime Sleep Aid (diphen)
diphenhydramine HCl	Nighttime Allergy Relief
diphenhydramine HCl	Ormir
diphenhydramine HCl	Pharbedryl
diphenhydramine HCl	Q-Dryl
diphenhydramine HCl	Quenalin
diphenhydramine HCl	Rest Simply Nighttime Sleep
diphenhydramine HCl	Restfully Sleep
diphenhydramine HCl	Siladryl SA
diphenhydramine HCl	Silphen Cough
diphenhydramine HCl	Simply Sleep
diphenhydramine HCl	Sleep
diphenhydramine HCl	Sleep Aid (diphenhydramine)
diphenhydramine HCl	Sleep Aid Max Str(diphenhydr)
diphenhydramine HCl	Sleep II
diphenhydramine HCl	Sleep Time
diphenhydramine HCl	Sleep-Tabs
diphenhydramine HCl	Sleeping
diphenhydramine HCl	Total Allergy Medicine
diphenhydramine HCl	Unisom SleepGels
diphenhydramine HCl	Unisom SleepMelts
diphenhydramine HCl	Valu-Dryl Allergy
diphenhydramine HCl	Vanamine PD
diphenhydramine HCl	Vicks QlearQuil Nighttime Rlf
diphenhydramine HCl	Wal-Dryl Allergy
diphenhydramine HCl	Wal-Sleep Z
diphenhydramine HCl	Wal-Som (diphenhydramine)
diphenhydramine HCl	Z-Sleep
diphenhydramine HCl	ZzzQuil
diphenhydramine HCl	diphenhydramine HCl
diphenhydramine HCl in 0.9 % sodium chloride	diphenhydramine-0.9 %sod.chlr
diphenhydramine HCl/hydrocortisone	HC Derma-Pax
diphenhydramine HCI/phenylephrine	Adult Robitussin Night M-SCId
HCI/acetaminophen	
diphenhydramine HCI/phenylephrine	Allergy M-S Nighttime
HCI/acetaminophen	
diphenhydramine HCI/phenylephrine	Allergy Plus Severe Sinus HA
HCI/acetaminophen	, mergy i las severe sinus in
diphenhydramine HCI/phenylephrine	Allergy Sinus Headache (PE)
HCI/acetaminophen	, mergy smas redudenc (i z)
nci/ acetaminophen	

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Generic Name	Brand Name
diphenhydramine HCl/phenylephrine	Allergy and Cold PE
HCl/acetaminophen	
diphenhydramine HCl/phenylephrine	Child Delsym Cough+Cold
HCl/acetaminophen	
diphenhydramine HCl/phenylephrine	Children Dimetapp M-SCold-Flu
HCl/acetaminophen	
diphenhydramine HCI/phenylephrine	Children's Mucinex NightTime
HCl/acetaminophen	
diphenhydramine HCl/phenylephrine	Cold and FluRelief(diphen-pe)
HCl/acetaminophen	
diphenhydramine HCl/phenylephrine	Cough and Severe Cold
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Delsym Cough-ColdNightTime
HCl/acetaminophen	
diphenhydramine HCI/phenylephrine	Flu Relief Therapy Nighttime
HCI/acetaminophen	Ι, Θ
diphenhydramine HCI/phenylephrine	Flu and Sore Throat Relief
HCI/acetaminophen	
diphenhydramine HCI/phenylephrine	Flu-Severe Cold-Cough Night
HCI/acetaminophen	
diphenhydramine HCI/phenylephrine	Herbiomed Allergy Cold-Sinus
HCI/acetaminophen	
diphenhydramine HCI/phenylephrine	Mucinex Fast-Max NiteCold-Flu
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Mucinex Sinus-Max NiteCongest
HCI/acetaminophen	0
diphenhydramine HCl/phenylephrine	Severe Allergy-SinusHeadache
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Severe Cold Cough-Flu
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Severe Cold PE
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Theraflu ExpressMax ColdNight
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Theraflu Night SevereCold-Cgh
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Theraflu Nighttime PowerPod
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Wal-Dryl Severe Allergy-Sinus
HCI/acetaminophen	114. 2. j. 3010.0 · mo. 6j. 0 m. 40
diphenhydramine HCl/phenylephrine	Wal-Flu Severe Cold andCough
HCI/acetaminophen	The transfer of a made ag.
diphenhydramine HCl/phenylephrine	Wal-phed PE Severe Cold
HCI/acetaminophen	114. p. 164. 1 500.0 00.4
diphenhydramine HCI/phenylephrine	Child Cold-Cough Day-Night
HCI/dextromethorphan HBr	5 55 55 54, 61.V
diphenhydramine	Sinus Relief Max StrDay-Night
HCl/phenylephrine/acetaminophen/guaifenesin	chiad hand mandel buy mane
diphenhydramine/phenylephrin/dextromethorph	Children's M-S ColdDay-Night
/acetaminophen/GG	
/ dectarimophen/ do	

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Generic Name	Brand Name
diphenhydramine/phenylephrin/dextromethorph	Daytime-ColdNighttime-Cld-Flu
/acetaminophen/GG	,
diphenhydramine/phenylephrin/dextromethorph	Mucinex Fast-Max Day-NiteCold
/acetaminophen/GG	,
diphenhydramine/phenylephrin/dextromethorph	Mucinex Fast-Max Day-NiteCong
/acetaminophen/GG	of the second of
doxylamine succ/pseudoephedrine	Glentuss
HCI/dextromethorphan Hbr	
doxylamine succ/pseudoephedrine	Lortuss DM
HCI/dextromethorphan Hbr	
doxylamine succinate/phenylephrine HCl	Poly Hist Forte
doxylamine succinate/phenylephrine HCl	Poly Hist Forte (doxylamine)
doxylamine succinate/phenylephrine HCl	doxylamine-phenylephrine
doxylamine succinate/pseudoephedrine HCl	Lortuss LO
doxylamine/phenylephrine/dextromethorphan	Day-Nite Severe Cold-Flu
/acetaminophen/GG	Day-INICE Severe Cold-11d
doxylamine/phenylephrine/dextromethorphan	Mucinex Fast-MaxDay-Nt(doxyl)
	Widelitex Tast-WaxDay-Nt(doxyl)
/acetaminophen/GG	Musings Cinus May Dv NH/dwyl)
doxylamine/phenylephrine/dextromethorphan	Mucinex Sinus-Max Dy-Nt(dxyl)
/acetaminophen/GG	Carrage Cald and Fly (Day (Night)
doxylamine/phenylephrine/dextromethorphan	Severe Cold andFlu(Day/Night)
/acetaminophen/GG	
dupilumab	Dupixent
dyphylline	Lufyllin
dyphylline	dyphylline (bulk)
emedastine difumarate	Emadine
ephedrine sulfate	ephedrine sulfate
ephedrine sulfate/guaifenesin	Bronkaid Dual Action
epinastine HCl	Elestat
epinastine HCl	epinastine
epinephrine	Adrenaclick
epinephrine	Adrenalin
epinephrine	Adyphren
epinephrine	Adyphren Amp
epinephrine	Adyphren Amp II
epinephrine	Adyphren II
epinephrine	Auvi-Q
epinephrine	Bronchial Mist
epinephrine	Bronchial Mist Refill
epinephrine	EPIsnap
epinephrine	EpiPen
epinephrine	EpiPen 2-Pak
epinephrine	EpiPen Jr
epinephrine	EpiPen Jr 2-Pak
epinephrine	EpinephrineSnap-EMS
epinephrine	EpinephrineSnap-V
epinephrine	Еру
epinephrine	Primatene Mist
epinephrine	Symjepi
epinephrine	epinephrine
epinephrine HCI/PF	epinephrine HCl (PF)
cpinepinine riciji i	epinepinine rior (i i j

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Canaria Nama	Drawd Name
Generic Name	Brand Name
fexofenadine HCl	Allegra Allergy
fexofenadine HCl	Aller-Fex
fexofenadine HCl	Aller-ease
fexofenadine HCl	Allergy Relief (fexofenadine)
fexofenadine HCl	Children's Allegra Allergy
fexofenadine HCl	Children's Allergy Relief(fex)
fexofenadine HCl	Children's Wal-Fex
fexofenadine HCl	Mucinex Allergy
fexofenadine HCl	Wal-Fex Allergy
fexofenadine HCl	fexofenadine
fexofenadine HCl	fexofenadine (bulk)
fexofenadine HCl/pseudoephedrine HCl	Allegra-D 12 Hour
fexofenadine HCl/pseudoephedrine HCl	Allegra-D 24 Hour
fexofenadine HCl/pseudoephedrine HCl	Allergy Relief D
fexofenadine HCI/pseudoephedrine HCI	Allergy Relief-D(fexofenadine)
fexofenadine HCI/pseudoephedrine HCI	Allergy-CongestRelief-D(fexo)
fexofenadine HCI/pseudoephedrine HCI	Wal-Fex D 12 Hour
fexofenadine HCl/pseudoephedrine HCl	Wal-Fex D 24 Hour
fexofenadine HCI/pseudoephedrine HCI	fexofenadine-pseudoephedrine
fludrocortisone acetate	fludrocortisone
flunisolide	Aerospan
flunisolide	flunisolide
fluocinolone acetonide/emollient combination	Synalar Cream Kit
no.65	
fluocinolone acetonide/emollient combination	Synalar Ointment Kit
no.65	
fluocinolone acetonide/skin cleanser comb no.28	Synalar TS
fluocinolone acetonide/skin cleanser	Xilapak
no.10/silicone, tape	
fluocinolone acetonide/urea/silicone, adhesive	Noxipak
flurbiprofen	flurbiprofen
fluticasone furoate	Arnuity Ellipta
fluticasone furoate	Children's Flonase Sensimist
fluticasone furoate	Flonase Sensimist
fluticasone furoate	Veramyst
fluticasone furoate/umeclidinium bromide/vilanterol	Trelegy Ellipta
trifenat	
fluticasone furoate/vilanterol trifenatate	Breo Ellipta
fluticasone propionate	24 Hour Allergy Relief
fluticasone propionate	Aller-Flo
fluticasone propionate	Allergy Relief (fluticasone)
fluticasone propionate	ArmonAir RespiClick
fluticasone propionate	Children's Flonase Allergy Rlf
fluticasone propionate	Childrens 24 Hr Allergy Relief
fluticasone propionate	ClariSpray
fluticasone propionate	Flonase
fluticasone propionate	Flonase Allergy Relief
fluticasone propionate	Flovent Diskus
fluticasone propionate	Flovent HFA
fluticasone propionate	Xhance
fluticasone propionate	fluticasone propionate
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Generic Name	Brand Name
fluticasone propionate	fluticasone propionate (bulk)
fluticasone propionate, micronized	fluticasone prop, micro (bulk)
fluticasone propionate/emollient combination	Beser Kit
no.65	
fluticasone propionate/salmeterol xinafoate	Advair Diskus
fluticasone propionate/salmeterol xinafoate	Advair HFA
fluticasone propionate/salmeterol xinafoate	AirDuo RespiClick
fluticasone propionate/salmeterol xinafoate	Wixela Inhub
fluticasone propionate/salmeterol xinafoate	fluticasone propion-salmeterol
fluticasone propionate/sodium chloride/sodium	Ticanase
bicarbonate	
fluticasone propionate/sodium chloride/sodium	Ticaspray
bicarbonate	
formoterol fumarate	Foradil Aerolizer
formoterol fumarate	Perforomist
formoterol fumarate	formoterol fumarate (bulk)
formoterol fumarate dihydrate, micronized	formoterol fum dihyd,mic(bulk)
glycopyrrolate	Seebri Neohaler
glycopyrrolate/formoterol fumarate	Bevespi Aerosphere
glycopyrrolate/nebulizer accessories	Lonhala Magnair Refill
glycopyrrolate/nebulizer and accessories	Lonhala Magnair Starter
guaifenesin/acetaminophen	Chest Congestion
guaifenesin/dextromethorphan HBr	Adt Robitussin Peak Cld DMMax
guaifenesin/dextromethorphan HBr	Adult Cough Formula DM Max
guaifenesin/dextromethorphan HBr	Adult Robitussin Peak ColdDM
guaifenesin/dextromethorphan HBr	Adult Tussin Cough CongestDM
guaifenesin/dextromethorphan HBr	Adult Tussin DM
guaifenesin/dextromethorphan HBr	Adult Wal-Tussin DM Max
guaifenesin/dextromethorphan HBr	Allfen DM
guaifenesin/dextromethorphan HBr	Biocotron
guaifenesin/dextromethorphan HBr	Biospec DMX
guaifenesin/dextromethorphan HBr	Chest Congestion Relief DM
guaifenesin/dextromethorphan HBr	Chest Congestion-CoughRelief
guaifenesin/dextromethorphan HBr	Child ChestCongestion-Cough
guaifenesin/dextromethorphan HBr	Child Cough-Chest CongestDM
guaifenesin/dextromethorphan HBr	Child Delsym Cough+ChestDM
guaifenesin/dextromethorphan HBr	Child Mucinex CoughMini-Melts
guaifenesin/dextromethorphan HBr	Child Mucus Relief Cough
guaifenesin/dextromethorphan HBr	Child TriaminicCough-Congest
guaifenesin/dextromethorphan HBr	Children's Cough
guaifenesin/dextromethorphan HBr	Children's Mucinex Cough
guaifenesin/dextromethorphan HBr	Chld Robitussin Cough-ChestDM
guaifenesin/dextromethorphan HBr	Coricidin HBP ChestCong-Cough
guaifenesin/dextromethorphan HBr	Cough Control DM
guaifenesin/dextromethorphan HBr	Cough Control DM Max
guaifenesin/dextromethorphan HBr	CoughSuppressant-Expectorant
guaifenesin/dextromethorphan HBr	Cough Syrup DM
guaifenesin/dextromethorphan HBr	Cough-Chest Congestion DM
guaifenesin/dextromethorphan HBr	DM Max
guaifenesin/dextromethorphan HBr	Daytime Mucus Relief DM
guaifenesin/dextromethorphan HBr	Delsym Cough-ChestCongest DM
guarieriesin/ dextrometrior priari ribi	Deisyili Cough-ChestCongest Divi

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Generic Name	Brand Name
guaifenesin/dextromethorphan HBr	Diabetic Siltussin-DM
guaifenesin/dextromethorphan HBr	Diabetic Siltussin-DM Max Str
guaifenesin/dextromethorphan HBr	Diabetic Tussin DM
guaifenesin/dextromethorphan HBr	Diabetic Tussin Max St
guaifenesin/dextromethorphan HBr	Double-Tussin DM
guaifenesin/dextromethorphan HBr	Expectorant DM
guaifenesin/dextromethorphan HBr	Fenesin DM IR
guaifenesin/dextromethorphan HBr	G-Fenesin DM
guaifenesin/dextromethorphan HBr	G-Tron
guaifenesin/dextromethorphan HBr	G-Zyncof
guaifenesin/dextromethorphan HBr	Geri-Tussin DM
guaifenesin/dextromethorphan HBr	Guaiasorb DM
guaifenesin/dextromethorphan HBr	Guaicon DMS
guaifenesin/dextromethorphan HBr	Guaifenesin-DM
guaifenesin/dextromethorphan HBr	Intense Cough
guaifenesin/dextromethorphan HBr	Intense Cough Reliever
guaifenesin/dextromethorphan HBr	Iophen DM-NR
guaifenesin/dextromethorphan HBr	Medi-Tussin DM
guaifenesin/dextromethorphan HBr	Medi-Tussin DM Diabetic
guaifenesin/dextromethorphan HBr	Mucinex DM
guaifenesin/dextromethorphan HBr	Mucinex Fast-Max DM Max
guaifenesin/dextromethorphan HBr	Mucosa DM
guaifenesin/dextromethorphan HBr	Mucus DM
guaifenesin/dextromethorphan HBr	Mucus DM Max ER
guaifenesin/dextromethorphan HBr	Mucus Relief Cough
guaifenesin/dextromethorphan HBr	Mucus Relief DM
guaifenesin/dextromethorphan HBr	Mucus Relief DM Cough
guaifenesin/dextromethorphan HBr	Mucus Relief DM Max
guaifenesin/dextromethorphan HBr	Mucus Relief ER DM-MAX
guaifenesin/dextromethorphan HBr	Mucus and Cough Relief
guaifenesin/dextromethorphan HBr	Neo-Tuss
guaifenesin/dextromethorphan HBr	Q-Tussin DM
guaifenesin/dextromethorphan HBr	Refenesen DM
guaifenesin/dextromethorphan HBr	Ri-Tussin DM
guaifenesin/dextromethorphan HBr	Robafen DM
guaifenesin/dextromethorphan HBr	Robafen DM Cough
guaifenesin/dextromethorphan HBr	Robafen DM Cough-ChestCongest
guaifenesin/dextromethorphan HBr	Robitussin Cough-ChestCong DM
guaifenesin/dextromethorphan HBr	Safe Tussin DM
guaifenesin/dextromethorphan HBr	Scot-Tussin Senior
guaifenesin/dextromethorphan HBr	Siltussin DM DAS
guaifenesin/dextromethorphan HBr	Siltussin-DM
guaifenesin/dextromethorphan HBr	Sorbugen NR
guaifenesin/dextromethorphan HBr	Supress DM
guaifenesin/dextromethorphan HBr	TRISPEC DMX
guaifenesin/dextromethorphan HBr	Tab Tussin DM
guaifenesin/dextromethorphan HBr	Tusnel Diabetic
guaifenesin/dextromethorphan HBr	Tussin Cough DM
guaifenesin/dextromethorphan HBr	Tussin Cough-ChestCongestion
guaifenesin/dextromethorphan HBr	Tussin DM
guaifenesin/dextromethorphan HBr	Tussin DM Clear

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Generic Name	Brand Name
guaifenesin/dextromethorphan HBr	Tussin DM Cough
guaifenesin/dextromethorphan HBr	Tussin DM Cough and Chest
guaifenesin/dextromethorphan HBr	Tussin DM Max
guaifenesin/dextromethorphan HBr	Ultra DM Free and Clear
guaifenesin/dextromethorphan HBr	Ultra Tuss Safe
guaifenesin/dextromethorphan HBr	Wal-Tussin DM
guaifenesin/dextromethorphan HBr	Zyncof
guaifenesin/dextromethorphan HBr	dextromethorphan-guaifenesin
guaifenesin/dextromethorphan HBr/phenylephrine	Actidom DMX
guaifenesin/dextromethorphan HBr/phenylephrine	Adult Robitussin M-S Cold
guaifenesin/dextromethorphan HBr/phenylephrine	Adult Robitussin Peak ColdM-S
guaifenesin/dextromethorphan HBr/phenylephrine	Adult Tussin Multi-Symp Cold
guaifenesin/dextromethorphan HBr/phenylephrine	Altipres
guaifenesin/dextromethorphan HBr/phenylephrine	Altipres Pediatric
guaifenesin/dextromethorphan HBr/phenylephrine	Aquanaz
guaifenesin/dextromethorphan HBr/phenylephrine	Bio T Pres
guaifenesin/dextromethorphan HBr/phenylephrine	Bio T Pres Pediatric
guaifenesin/dextromethorphan HBr/phenylephrine	Bio-S-Pres Dx
guaifenesin/dextromethorphan HBr/phenylephrine	BioGtuss NF
guaifenesin/dextromethorphan HBr/phenylephrine	Biobron DX
guaifenesin/dextromethorphan HBr/phenylephrine	Biobron SF
guaifenesin/dextromethorphan HBr/phenylephrine	Biocotron-D
guaifenesin/dextromethorphan HBr/phenylephrine	Biodesp DM
guaifenesin/dextromethorphan HBr/phenylephrine	Biogil
guaifenesin/dextromethorphan HBr/phenylephrine	Broncotron PED
guaifenesin/dextromethorphan HBr/phenylephrine	Brontuss SF
guaifenesin/dextromethorphan HBr/phenylephrine	Child MucinexCongestion-Cough
guaifenesin/dextromethorphan HBr/phenylephrine	Child Multi-SymptomCold/Cough
guaifenesin/dextromethorphan HBr/phenylephrine	Child's Mucus Relief M-S Cold
guaifenesin/dextromethorphan HBr/phenylephrine	Children's MucinexMulti-Symp
guaifenesin/dextromethorphan HBr/phenylephrine	Cough Control CF (PE)
guaifenesin/dextromethorphan HBr/phenylephrine	Cough and Cold
guaifenesin/dextromethorphan HBr/phenylephrine	Cough and Cold Mucus ReliefCF
guaifenesin/dextromethorphan HBr/phenylephrine	Deconex DMX
guaifenesin/dextromethorphan HBr/phenylephrine	Desgen DM
guaifenesin/dextromethorphan HBr/phenylephrine guaifenesin/dextromethorphan HBr/phenylephrine	Desgen DM
• • • • • •	Despec DM-G
guaifenesin/dextromethorphan HBr/phenylephrine	Despec EDA Cough-ColdDrops
guaifenesin/dextromethorphan HBr/phenylephrine	Despec-DM(phenyleph-DM-guaif)
guaifenesin/dextromethorphan HBr/phenylephrine	Dometuss-DMX
guaifenesin/dextromethorphan HBr/phenylephrine	Duravent DM
guaifenesin/dextromethorphan HBr/phenylephrine	Endacon
guaifenesin/dextromethorphan HBr/phenylephrine	Exactuss
guaifenesin/dextromethorphan HBr/phenylephrine	Exact uss TR
guaifenesin/dextromethorphan HBr/phenylephrine	Fast Mucus RlfCongest-Cough
guaifenesin/dextromethorphan HBr/phenylephrine	G-Supress DX
guaifenesin/dextromethorphan HBr/phenylephrine	G-Tron PED
guaifenesin/dextromethorphan HBr/phenylephrine	G-Tusicof
guaifenesin/dextromethorphan HBr/phenylephrine	Giltuss
guaifenesin/dextromethorphan HBr/phenylephrine	Giltuss Cough-Cold
guaifenesin/dextromethorphan HBr/phenylephrine	Giltuss Pediatric

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Generic Name	Brand Name
guaifenesin/dextromethorphan HBr/phenylephrine	Giltuss TR
guaifenesin/dextromethorphan HBr/phenylephrine	Maxiphen DM
guaifenesin/dextromethorphan HBr/phenylephrine	Mucinex Fast-MaxCongest-Cough
guaifenesin/dextromethorphan HBr/phenylephrine	Mucus ReliefCongestion-Cough
guaifenesin/dextromethorphan HBr/phenylephrine	NeoTuss-D (ImprovedFormula)
guaifenesin/dextromethorphan HBr/phenylephrine	Nivanex DMX
guaifenesin/dextromethorphan HBr/phenylephrine	Pres Gen
guaifenesin/dextromethorphan HBr/phenylephrine	Pres Gen Pediatric
guaifenesin/dextromethorphan HBr/phenylephrine	Relhist DMX
guaifenesin/dextromethorphan HBr/phenylephrine	Robafen CF (phenylephrine)
guaifenesin/dextromethorphan HBr/phenylephrine	Robitussin Cough and ColdCF
guaifenesin/dextromethorphan HBr/phenylephrine	Robitussin M-S Cold CF Max
guaifenesin/dextromethorphan HBr/phenylephrine	Severe Congestion and Cough Max
guaifenesin/dextromethorphan HBr/phenylephrine	Supress DX
guaifenesin/dextromethorphan HBr/phenylephrine	Tusicof
guaifenesin/dextromethorphan HBr/phenylephrine	Tusnel DM
guaifenesin/dextromethorphan HBr/phenylephrine	Tusnel DMPediatric(phenyleph)
guaifenesin/dextromethorphan HBr/phenylephrine	Tussi-Pres
guaifenesin/dextromethorphan HBr/phenylephrine	Tussi-Pres Pediatric
guaifenesin/dextromethorphan HBr/phenylephrine	Tussin CF (PE-DM-guaif)
guaifenesin/dextromethorphan HBr/phenylephrine	Tussin CF Cough-Cold
guaifenesin/dextromethorphan HBr/phenylephrine	Tussin CF MAX
guaifenesin/dextromethorphan HBr/phenylephrine	Tusslin
guaifenesin/dextromethorphan HBr/phenylephrine	VanaTab DM
guaifenesin/dextromethorphan HBr/phenylephrine	Vanacof DM
guaifenesin/dextromethorphan HBr/phenylephrine	Wal-Tussin Cough and ColdCF
guaifenesin/dextromethorphan HBr/phenylephrine	phenylephrine-DM-guaifenesin
guaifenesin/dextromethorphan HBr/potassium	Sorbutuss
citrate	
guaifenesin/dextromethorphan	Actinel
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Actinel Pediatric
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Ambi 40PSE-400GFN-20DM
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Bionel
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Bionel Pediatric
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Capmist DM
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Desgen DM(pseudoephedrine)
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Despec-DM(pseudoeph-DM-guaif)
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Entex PAC
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	Entre-Cough
HBr/pseudoephedrine HCl	
guaifenesin/dextromethorphan	ExeFen DMX
HBr/pseudoephedrine HCl	

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sualfenesin/dextromethorphan HBr/pseudoephedrine HCl guafenesin/dextromethorphan HBr/pseudoephedrine HCl guafenesin/deyhedrine HCl guafenesin/dephedrine HCl guafenesin/deyhodeodne bitartrate guafenesin/deyhodeodne bitartrate guafenesin/dephedrine HCl guafenesin/deyhodeodne bitartrate guafenesin/phenylephrine HCl Guafen	Generic Name	Brand Name
iBB/pseudoephedrine HCI gualfenesin/dextromethorphan HB/pseudoephedrine HCI gualfenesin/dybylline gualfenesin/dybylline Ufilia 400 gualfenesin/dybylline gualfenesin/dybylorocodone bitartrate gualfenesin/dybrocodone bitartrate gualfenesin/phrocodone bitartrate gualfenesin/phenylephrine HCI		
gualfenesin/dextromethorphan HBr/pseudoephedrine HCl gualfenesin/dybrylline gualfenesin/dybrylline gualfenesin/dybrylline gualfenesin/dybrylline gualfenesin/dybrylline gualfenesin/phorocodone bitartrate gualfenesin/phorocodone bitartrate gualfenesin/phenylephrine HCl Gualfenesin/phenylephrine	•	0
HB/pseudoephedrine HCl guaifenesin/dextromethorphan Robafen CF HB/pseudoephedrine HCl guaifenesin/dextromethorphan TRISPEC PSE HB/pseudoephedrine HCl guaifenesin/dextromethorphan Tusnel DMPediatric(pseudoeph) HB/pseudoephedrine HCl guaifenesin/dextromethorphan Tusnel New Formula HB/pseudoephedrine HCl guaifenesin/dextromethorphan Tusnel New Formula HB/pseudoephedrine HCl guaifenesin/dextromethorphan Tusnel Pediatric guaifenesin/dextromethorphan Tusnel Pediatric HB/pseudoephedrine HCl guaifenesin/dybhylline Difil-G 400 guaifenesin/dybhylline Difil-G 400 guaifenesin/hydrocodone bitartrate Flowtuss guaifenesin/phenylephrine HCl Primatene Asthma guaifenesin/phenylephrine HCl Chest Congestion Relief PE guaifenesin/phenylephrine HCl Chest Congestion Relief PE guaifenesin/phenylephrine HCl Chest Congestion Relief PE guaifenesin/phenylephrine HCl Child Mucinex StuffyNose-Cold guaifenesin/phenylephrine HCl Child Mucinex StuffyNose-Cold guaifenesin/phenylephrine HCl Child Mucinex StuffyNose-Cold guaifenesin/phenylephrine HCl Despec guaifenesin/phenylephrine HCl Despec guaifenesin/phenylephrine HCl Despec guaifenesin/phenylephrine HCl Gilphex TR guaifenesin/phenylephrine HCl Gilphex TR guaifenesin/phenylephrine HCl Gilphex TR guaifenesin/phenylephrine HCl Gilphex TR guaifenesin/phenylephrine HCl Hours of Penesin PE IR guaifenesin/phenylephrine HCl Hours of PE guaifenesin/phenylephrine		Poly-Vent DM
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guaifenesin/phepherine HCl guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/phenylephrine HCl guaifenesin/ph	•	Z-COT 12 DIVI
guaifenesin/ephedrine HCl guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/phdrocodone bitartrate guaifenesin/phenylephrine HCl guaifenesin/phe		D:EI C 400
guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/hydrocodone bitartrate guaifenesin/phenylephrine HCl guaifenesin/phenyleph		
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guaifenesin/hydrocodone bitartrate guaifenesin/phenylephrine HCI g		
guaifenesin/phenylephrine HCl guaife		
guaifenesin/phenylephrine HCl guaife		
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guaifenesin/phenylephrine HCl guaife	_	•
guaifenesin/phenylephrine HCl guaife		_
guaifenesin/phenylephrine HCl Guaife	_	Deconex IR
guaifenesin/phenylephrine HCl Supress-PE guaifenesin/phenylephrine HCl Guaifenesin/phenylephrine		•
guaifenesin/phenylephrine HCl	_	Duravent PE
guaifenesin/phenylephrine HCl Guaife	_	ED Bron GP
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	Entex LQ
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	ExaPhex TR
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	Fenesin PE IR
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	Gilphex TR
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	J-MAX
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	Liquibid D-R
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	Liquibid PD-R
guaifenesin/phenylephrine HCl	guaifenesin/phenylephrine HCl	Maxiphen
guaifenesin/phenylephrine HCl TL-DMX	guaifenesin/phenylephrine HCl	MucaphEd
guaifenesin/phenylephrine HCl Mucus Relief Sinus guaifenesin/phenylephrine HCl Refenesen PE guaifenesin/phenylephrine HCl Rescon-GG guaifenesin/phenylephrine HCl Supress-PE guaifenesin/phenylephrine HCl TL-DMX	guaifenesin/phenylephrine HCl	Mucus Relief D(phenylephrine)
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guaifenesin/phenylephrine HCl Supress-PE guaifenesin/phenylephrine HCl TL-DMX	_	
guaifenesin/phenylephrine HCl TL-DMX		
		·
	guaifenesin/phenylephrine HCl/acetaminophen	Cold HeadCongest(gg-pe-acetm)

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Generic Name	Brand Name
guaifenesin/phenylephrine HCl/acetaminophen	Mucinex Cold and Sinus
guaifenesin/phenylephrine HCl/acetaminophen	Mucinex Fast-Max Cold-Sinus
guaifenesin/phenylephrine HCl/acetaminophen	Mucinex Sinus-MaxPressur-Pain
guaifenesin/phenylephrine HCl/acetaminophen	Mucinex Sinus-Max SevCongestn
guaifenesin/phenylephrine HCl/acetaminophen	Mucus Relief Cold and Sinus
guaifenesin/phenylephrine HCl/acetaminophen	Mucus ReliefSinusPressur-Pain
guaifenesin/phenylephrine HCl/acetaminophen	Mucus RIf Severe SinusCongest
guaifenesin/phenylephrine HCl/acetaminophen	Pressure-Pain PE Plus Mucus
guaifenesin/phenylephrine HCl/acetaminophen	Severe Congestion Relief
guaifenesin/phenylephrine HCl/acetaminophen	Severe Sinus
guaifenesin/phenylephrine HCl/acetaminophen	Sinus Congestion-Pain(guaif)
guaifenesin/phenylephrine HCl/acetaminophen	Sinus Relief Pressure and Pain
guaifenesin/phenylephrine HCl/acetaminophen	Sinus Relief SevereCongestion
guaifenesin/phenylephrine HCl/acetaminophen	Sudafed PEPressure-Pain-Mucus
guaifenesin/phenylephrine HCl/acetaminophen	Tylenol Cold Head CongestSevr
guaifenesin/phenylephrine HCl/acetaminophen	Tylenol Sinus CongestionPain
guaifenesin/phenylephrine HCl/acetaminophen	Tylenol Sinus Severe
guaifenesin/pseudoephedrine HCl	Ambi 60PSE-400GFN
guaifenesin/pseudoephedrine HCl	Chest Congestion Relief D
guaifenesin/pseudoephedrine HCl	
•	Congest-Eze
guaifenesin/pseudoephedrine HCl	Congestac
guaifenesin/pseudoephedrine HCl	Despec-Tab
guaifenesin/pseudoephedrine HCl	Entex T ExeFen-IR
guaifenesin/pseudoephedrine HCl	Maxifed
guaifenesin/pseudoephedrine HCl	
guaifenesin/pseudoephedrine HCl	Mucinex D
guaifenesin/pseudoephedrine HCl	Mucinex D Maximum Strength
guaifenesin/pseudoephedrine HCl	Mucus D
guaifenesin/pseudoephedrine HCl	Mucus Relief D(pseudoephed)
guaifenesin/pseudoephedrine HCl	Poly-Vent IR
guaifenesin/pseudoephedrine HCl	Respaire-30
guaifenesin/pseudoephedrine HCl	Triacting Expectorant
guaifenesin/pseudoephedrine HCl	Tusnel Pediatric
guaifenesin/pseudoephedrine HCl	pseudoephedrine-guaifenesin
halobetasol propionate/ammonium lactate	Halonate
halobetasol propionate/ammonium lactate	Halonate Pac
halobetasol propionate/ammonium lactate	Ultravate PAC
halobetasol propionate/lactic acid	Ultravate X
hydrocodone bitartrate/chlorpheniramine maleate	Vituz
hydrocodone bitartrate/homatropine	Hydrocodone Compound
methylbromide	
hydrocodone bitartrate/homatropine	Hydromet
methylbromide	
hydrocodone bitartrate/homatropine	Tussigon
methylbromide	
hydrocodone bitartrate/homatropine	hydrocodone-homatropine
methylbromide	
hydrocodone bitartrate/pseudoephedrine	Hycofenix
HCI/guaifenesin	
hydrocodone polistirex/chlorpheniramine polistirex	TussiCaps
hydrocodone polistirex/chlorpheniramine polistirex	Tussionex Pennkinetic ER

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Generic Name	Brand Name
hydrocodone polistirex/chlorpheniramine polistirex	hydrocodone-chlorpheniramine
hydrocortisone	Cortef
hydrocortisone	hydrocortisone
hydrocortisone acetate/aloe vera	Nucort
hydrocortisone acetate/aloe vera	hydrocortisone acet-aloe vera
hydrocortisone acetate/pramoxine HCl	, Analpram-HC
hydrocortisone acetate/pramoxine HCl	Epifoam
hydrocortisone acetate/pramoxine HCl	Mezparox-HC
hydrocortisone acetate/pramoxine HCl	Novacort
hydrocortisone acetate/pramoxine HCl	Pramosone
hydrocortisone acetate/pramoxine HCl	hydrocortisone-pramoxine
hydrocortisone acetate/pramoxine HCl/aloe	Novacort (with aloe)
polysaccharide	
hydrocortisone acetate/pramoxine HCI/emollient	Pramosone E
base	
hydrocortisone acetate/urea	U-Cort
hydrocortisone sod succinate	A-Hydrocort
hydrocortisone sod succinate	Solu-Cortef
hydrocortisone sodium succinate/PF	Solu-Cortef Act-O-Vial (PF)
hydrocortisone/aloe vera	Anti-Itch(hydrocortisone)-Aloe
hydrocortisone/aloe vera	Cortisone with Aloe
hydrocortisone/aloe vera	Cortizone-10 with aloe
hydrocortisone/aloe vera	Hydrocortisone Plus
hydrocortisone/aloe vera	, Hydroskin with Aloe
hydrocortisone/aloe vera	hydrocortisone-aloe vera
hydrocortisone/aloe vera/vitamin E	Anti-Itch (HC) with Aloe-Vit E
acetate/vitamins A and D	. ,
hydrocortisone/aloe vera/vitamin E	Anti-Itch Plus
acetate/vitamins A and D	
hydrocortisone/emollient combination no.45	Pediaderm HC
hydrocortisone/mineral oil/petrolatum,white	hydrocortisone-min oil-wht pet
hydrocortisone/skin cleanser combination no.25	Aqua Glycolic HC
hydrocortisone/skin cleanser combination no.35	Dermasorb HC Complete Kit
ibuprofen	Addaprin
ibuprofen	Children's Ibu-Drops
ibuprofen	Children's Ibuprofen
ibuprofen	Ibuprofen IB
ibuprofen	Ibuprofen Jr Strength
ibuprofen	Infant's Ibuprofen
ibuprofen	Infants Ibu-Drops
ibuprofen	Medi-Profen
ibuprofen	Wal-Profen
ibuprofen	ibuprofen
ibuprofen/diphenhydramine HCl	Ibuprofen PM
ibuprofen/diphenhydramine HCl	ibuprofen-diphenhydramineHCl
ibuprofen/diphenhydramine citrate	Ibuprofen PM
ibuprofen/phenylephrine HCl	Advil Congestion Relief
ibuprofen/phenylephrine HCl	Congestion Relief(ibuprof-PE)
ibuprofen/pseudoephedrine HCl	Advil Cold and Sinus
ibuprofen/pseudoephedrine HCl	Cold and Sinus Pain Relief
ibuprofen/pseudoephedrine HCl	Cold-Sinus Relief

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Generic Name	Brand Name
ibuprofen/pseudoephedrine HCl	Ibuprofen Cold
ibuprofen/pseudoephedrine HCl	Ibuprofen Cold-Sinus(withPSE)
ibuprofen/pseudoephedrine HCl	Wal-Profen Cold-Sinus
ibuprofen/pseudoephedrine HCl	Wal-Profen D Cold and Sinus
indacaterol maleate	Arcapta Neohaler
indacaterol maleate/glycopyrrolate	Utibron Neohaler
ipratropium bromide	Atrovent HFA
ipratropium bromide	ipratropium bromide
ipratropium bromide/albuterol sulfate	Combivent Respimat
ipratropium bromide/albuterol sulfate	DuoNeb
ipratropium bromide/albuterol sulfate	ipratropium-albuterol
ketotifen fumarate	Alaway
ketotifen fumarate	Allergy Eye (ketotifen)
ketotifen fumarate	Antihistamine Eye Drops
ketotifen fumarate	Children's Alaway
ketotifen fumarate	Eye Itch Relief
ketotifen fumarate	Itchy Eye Drops
ketotifen fumarate	Wal-Zyr (ketotifen)
ketotifen fumarate	Zaditor
ketotifen fumarate	ketotifen fumarate
levalbuterol HCl	Xopenex
levalbuterol HCl	Xopenex Concentrate
levalbuterol HCl	levalbuterol HCl
levalbuterol HCl	levalbuterol HCl (bulk)
levalbuterol tartrate	Xopenex HFA
levalbuterol tartrate	levalbuterol tartrate
levocetirizine dihydrochloride	24HR Allergy Relief
levocetirizine dihydrochloride	Xyzal
levocetirizine dihydrochloride	levocetirizine
levocetirizine dihydrochloride	levocetirizine (bulk)
lodoxamide tromethamine	Alomide
loratadine	Alavert
loratadine	Allerclear
loratadine	Allergy Relief (loratadine)
loratadine	Children's Allergy Relief(lor)
loratadine	Children's Claritin
loratadine	Children's Loratadine
loratadine	Claritin
loratadine	Claritin Liqui-Gel
loratadine	Claritin RediTabs
loratadine	Loradamed
loratadine	Non-Drowsy Allergy
loratadine	Vicks QlearQuil Allergy
loratadine	Wal-itin
loratadine	loratadine
loratadine	loratadine (bulk)
loratadine, micronized	loratadine, micronized (bulk)
loratadine/pseudoephedrine sulfate	Alavert D-12 Allergy-Sinus
loratadine/pseudoephedrine sulfate	AllerClear D-12hr
loratadine/pseudoephedrine sulfate	AllerClear D-24hr
loratadine/pseudoephedrine sulfate	Allergy Relief D-24hr
iorataanie, pocaaocpiicarine sanate	Aller by Teller D ZTIII

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Generic Name	Brand Name
loratadine/pseudoephedrine sulfate	Allergy Relief D12
loratadine/pseudoephedrine sulfate	Allergy Relief, Nasal Decongest
loratadine/pseudoephedrine sulfate	Allergy Relief-D (loratadine)
loratadine/pseudoephedrine sulfate	Allergy and Congestion Relief
loratadine/pseudoephedrine sulfate	Allergy-Congestion Relief-D
loratadine/pseudoephedrine sulfate	Claritin-D 12 Hour
loratadine/pseudoephedrine sulfate	Claritin-D 24 Hour
loratadine/pseudoephedrine sulfate	Lorata-D
loratadine/pseudoephedrine sulfate	Loratadine-D
loratadine/pseudoephedrine sulfate	Wal-Itin D 12 Hour
loratadine/pseudoephedrine sulfate	Wal-itin D
loratadine/pseudoephedrine sulfate	lorata-dine D
loratadine/pseudoephedrine sulfate	loratadine-pseudoephedrine
meloxicam	Mobic
meloxicam	meloxicam
mepolizumab	Nucala
metaproterenol sulfate	metaproterenol
methylprednisolone	Medrol
methylprednisolone	Medrol (Pak)
methylprednisolone	Methylpred DP
methylprednisolone	methylprednisolone
methylprednisolone acetate	Depo-Medrol
methylprednisolone acetate	P-Care D40
methylprednisolone acetate	P-Care D80
methylprednisolone acetate	ReadySharpMethylprednisolone
methylprednisolone acetate	methylprednisolone acetate
methylprednisolone acetate in sodium	methylpredac(PF)-NaCl,iso-osm
chloride,iso-osmotic/PF	
methylprednisolone acetate in sterile water for	methylprednisoloneacet-water
injection	
methylprednisolone acetate/bupivacaine HCl	Physicians EZ Use M-Pred
methylprednisolone acetate/bupivacaine HCl in	methylprednisolac-bupivac-wat
sterile water	, ,
methylprednisolone acetate/norflurane/HFC 245fa	Medroloan II SUIK
methylprednisolone acetate/norflurane/HFC 245fa	Medroloan SUIK
methylprednisolone acetate/norflurane/HFC 245fa	P-Care D40G
methylprednisolone acetate/norflurane/HFC 245fa	P-Care D80G
methylprednisolone sodium succinate	Solu-Medrol
methylprednisolone sodium succinate	methylprednisolone sodiumsucc
methylprednisolone sodium succinate/PF	Solu-Medrol (PF)
methylprednisolone, micronized	methylprednisolone, mic(bulk)
mometasone furoate	Asmanex HFA
mometasone furoate	Asmanex Twisthaler
mometasone furoate	Nasonex
mometasone furoate	mometasone
mometasone furoate	mometasone furoate (bulk)
mometasone furoate/ammonium lactate	Momexin
	Dulera
·	
mometasone furoate/formoterol fumarate montelukast sodium montelukast sodium montelukast sodium	

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Generic Name	Brand Name
naproxen	naproxen
naproxen sodium	All Day Pain Relief
naproxen sodium	All Day Relief
naproxen sodium	Flanax (naproxen)
naproxen sodium	Midol (naproxen)
naproxen sodium	Wal-Proxen
naproxen sodium	naproxen sodium
naproxen sodium/pseudoephedrine HCl	Aleve Cold and Sinus
naproxen sodium/pseudoephedrine HCl	Aleve Sinus and Headache
naproxen sodium/pseudoephedrine HCl	All Day Pain Relief Sinus,Cold
naproxen sodium/pseudoephedrine HCl	Sinus and Cold-D
nedocromil sodium	Alocril
olodaterol HCl	Striverdi Respimat
olopatadine HCl	Pataday
olopatadine HCl	Patanase
olopatadine HCl	Patanol
olopatadine HCl	Pazeo
olopatadine HCl	olopatadine
omalizumab	Xolair
phenylephrine HCI/acetaminophen	AcetaminophenCongestion-Pain
phenylephrine HCl/acetaminophen	Contac Cold-Flu Day
phenylephrine HCl/acetaminophen	DayTime Sinus
phenylephrine HCl/acetaminophen	Daytime Sinus-Congestion
phenylephrine HCl/acetaminophen	Mapap Sinus Max Strength(PE)
phenylephrine HCl/acetaminophen	Non-Aspirin Sinus
phenylephrine HCl/acetaminophen	Pain Relief Sinus PE
phenylephrine HCl/acetaminophen	Pyrroxate Cold andCongestion
phenylephrine HCl/acetaminophen	Sinus Congestion and Pain
phenylephrine HCl/acetaminophen	Sinus Headache PE
phenylephrine HCl/acetaminophen	Sinus Maximum Strength
phenylephrine HCl/acetaminophen	Sinus Pain-Pressure (PE)
phenylephrine HCl/acetaminophen	Sinus Relief (Non-Drowsy)
phenylephrine HCl/acetaminophen	Sudafed PE Pressure-Pain
phenylephrine HCl/acetaminophen	Suphedrine PE SinusHeadache
phenylephrine HCl/acetaminophen	Tylenol Sinus CongestionPain
phenylephrine HCl/acetaminophen	Vicks Dayquil Sinex
phenylephrine HCl/acetaminophen	Vicks QlearQuil DaytimeSinus
phenylephrine HCl/acetaminophen	Vicks Sinex Daytime Vicks Sinex Daytime
phenylephrine HCl/acetaminophen	Wal-Phed PE SinusHeadache
phenylephrine	Allergy Multi-Symptom
	Allergy Multi-Symptom
HCl/acetaminophen/chlorpheniramine phenylephrine	Allergy Relief Multi-Symptom
	Allergy Relief Multi-Symptom
HCl/acetaminophen/chlorpheniramine	Alleray Delief/chlerahon cost)
phenylephrine	Allergy Relief(chlorphen-acet)
HCI/acetaminophen/chlorpheniramine	Alloray Sinus DE
phenylephrine	Allergy Sinus PE
HCl/acetaminophen/chlorpheniramine	Courtes Cold Eliz Dozzan delinia
phenylephrine	Contac Cold-Flu Day and Night
HCl/acetaminophen/chlorpheniramine	Cantas Cald Eli. May Chronath
phenylephrine	Contac Cold-Flu Max Strength
HCl/acetaminophen/chlorpheniramine	

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Generic Name	Brand Name
phenylephrine	Dristan Cold
HCl/acetaminophen/chlorpheniramine	Shotan colu
phenylephrine	Effervescent Cold Relief Plus
HCl/acetaminophen/chlorpheniramine	
phenylephrine	Medicidin-D
HCl/acetaminophen/chlorpheniramine	
phenylephrine	Norel AD
HCl/acetaminophen/chlorpheniramine	
phenylephrine	Sinus Congest-PainDay-Night
HCI/acetaminophen/chlorpheniramine	, ,
phenylephrine	SinusCongestion-Pain(chlorph)
HCl/acetaminophen/chlorpheniramine	. , ,
phenylephrine	Sinutrol PE
HCl/acetaminophen/chlorpheniramine	
phenylephrine HCl/acetaminophen/doxylamine	DayTime and NiteTime Sinus
succinate	
phenylephrine HCI/acetaminophen/doxylamine	NightTime Sinus
succinate	
phenylephrine HCI/acetaminophen/doxylamine	Nighttime Sinus-Congestion
succinate	
phenylephrine HCI/acetaminophen/doxylamine	Sinus Daytime-Nightime
succinate	
phenylephrine HCI/acetaminophen/doxylamine	Vicks Nyquil Sinex
succinate	
phenylephrine HCI/acetaminophen/doxylamine	Vicks QlearQuil NightimeSinus
succinate	
phenylephrine HCI/chlophedianol HCI/guaifenesin	Donatussin Pediatric
phenylephrine HCI/chlophedianol HCI/guaifenesin	Vanacof GPE
phenylephrine HCI/chlophedianol HCI/guaifenesin	phenylephrine-chlophedianol-GG
phenylephrine HCI/codeine	Phenflu CD
phosphate/acetaminophen/guaifen	
phenylephrine HCI/codeine	Phenflu CDX
phosphate/acetaminophen/guaifen	
phenylephrine HCI/dextromethorphan	Children's Cold-Cough-Sore
HBr/acetaminophen/guaifen	
phenylephrine HCl/dextromethorphan	Children's MucinexCold-Fever
HBr/acetaminophen/guaifen	
phenylephrine HCl/dextromethorphan	Cold Head Congestion SeverDay
HBr/acetaminophen/guaifen	
phenylephrine HCI/dextromethorphan	Cold Severe Congestion
HBr/acetaminophen/guaifen	0 11 151 6
phenylephrine HCI/dextromethorphan	Cold and Flu Severe
HBr/acetaminophen/guaifen	0.110 1.01 0.11.105
phenylephrine HCI/dextromethorphan	Cold-Cough Sinus Relief PE
HBr/acetaminophen/guaifen	Decarel Forte Plus
phenylephrine HCl/dextromethorphan	Decorel Forte Plus
HBr/acetaminophen/guaifen	Doloum Cough Cold Douting
phenylephrine HCI/dextromethorphan	Delsym Cough-Cold Daytime
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Dometuss G
	סטווופנמפפ מ
HBr/acetaminophen/guaifen	

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Generic Name	Brand Name
henylephrine HCl/dextromethorphan	Fast Mucus Relief SevereCold
lBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Head Congestion Cold Relief
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Herbiomed Severe Cold-FluM-S
lBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Mucinex Cold,Flu,Sore Throat
HBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Mucinex Fast-MaxCold-Flu-Thrt
IBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Mucinex Fast-Max SevereCold
IBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Mucinex Sinus-MaxPressure-Cgh
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Mucinex Sinus-Max SevCong(DM)
IBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Mucus Relief Cold-Flu-SoreThr
IBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Mucus Relief Plus
IBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Mucus Relief SevCongest-Cold
Br/acetaminophen/guaifen	ŭ
henylephrine HCl/dextromethorphan	Mucus Relief Severe Cold
IBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Multi-Symptom Cold (PE)
IBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Non-Pseudo Cold Relief
IBr/acetaminophen/guaifen	Non i seddo cola Nellei
shenylephrine HCl/dextromethorphan	Pain Relief Cold
HBr/acetaminophen/guaifen	Taill Neller Cold
shenylephrine HCI/dextromethorphan	Pressure-Pain PE Plus Cold
HBr/acetaminophen/guaifen	riessuie-raili re rius colu
phenylephrine HCI/dextromethorphan	Pressure-Pain-Cold
• •	riessuie-raiii-coid
HBr/acetaminophen/guaifen	Domino Docho May MultiCumortamo
henylephrine HCl/dextromethorphan	Rompe Pecho Max MultiSymptoms
HBr/acetaminophen/guaifen	Course Cold
henylephrine HCl/dextromethorphan	Severe Cold
IBr/acetaminophen/guaifen	C C LIAA IV C
henylephrine HCl/dextromethorphan	Severe Cold Multi-Symptom
IBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Severe Cold and Flu (PE)
IBr/acetaminophen/guaifen	0.16.1959
henylephrine HCI/dextromethorphan	Sudafed PEPressure-Pain-Cold
IBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Tussin CF Max Severe M-SCold
IBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Tylenol Cold and Flu Severe
IBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Vicks DayQuil SevereCold-Flu
IBr/acetaminophen/guaifen	

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Generic Name	Brand Name
phenylephrine HCl/dextromethorphan	Wal-Phed PE Cold-Cough
HBr/acetaminophen/guaifen	Wall filed i E cold cough
phenylephrine HCl/dextromethorphan	Wal-Phed PEPressure+Pain+Cold
HBr/acetaminophen/guaifen	
phenylephrine HCl/diphenhydramine HCl	Aldex-CT
phenylephrine HCl/diphenhydramine HCl	Allergy and Sinus Relief
phenylephrine HCl/diphenhydramine HCl	Child Allergy Plus Congestion
phenylephrine HCl/diphenhydramine HCl	Child Benadryl PlusCongestion
phenylephrine HCl/diphenhydramine HCl	Child's Benadryl-D Allergy-Sin
phenylephrine HCl/diphenhydramine HCl	Children Night TimeCold-Cough
phenylephrine HCl/diphenhydramine HCl	Childs Triacting Cold-Cough
phenylephrine HCl/diphenhydramine HCl	Cold and Cough(diphenhydr-pe)
phenylephrine HCl/diphenhydramine HCl	Dimetapp Cold-Congestion
phenylephrine HCl/diphenhydramine HCl	Nighttime Cough-Cold
phenylephrine HCl/diphenhydramine HCl	Triaminic Cold andCoughNT(PE)
phenylephrine HCl/diphenhydramine HCl	diphenhydramine-phenylephrine
phenylephrine HCl/promethazine HCl	Promethazine VC
phenylephrine HCl/promethazine HCl	promethazine-phenylephrine
phenylephrine HCl/pyrilamine maleate	Aldex D
phenylephrine HCl/pyrilamine maleate	Glen PE
phenylephrine HCl/pyrilamine maleate	Poly Hist Forte (pyrilamine)
phenylephrine HCl/pyrilamine maleate	Pyril D
phenylephrine HCl/pyrilamine maleate	, Vazotab (pyrilamine)
phenylephrine HCl/pyrilamine maleate	pyrilamine-phenylephrine
phenylephrine HCl/triprolidine HCl	Histex PE
phenylephrine HCl/triprolidine HCl	Sinus Nighttime
prednisolone	Millipred
prednisolone	Millipred DP
prednisolone	Prelone
prednisolone	prednisolone
prednisolone acetate	Flo-Pred
prednisolone acetate, micronized	prednisolone ac, micro (bulk)
prednisolone, micronized	prednisolone, micro (bulk)
prednisone	Deltasone
prednisone	Prednisone Intensol
prednisone	Rayos
prednisone	prednisone
prednisone micronized	prednisone micronized (bulk)
promethazine HCl	Phenadoz
promethazine HCl	Phenergan
promethazine HCl	Promethegan
promethazine HCl	promethazine
promethazine HCl	promethazine (bulk)
promethazine HCl in 0.9 % sodium chloride	promethazine in 0.9 % NaCl
promethazine HCI/codeine	promethazine-codeine
promethazine HCl/dextromethorphan HBr	promethazine-DM
promethazine/phenylephrine HCl/codeine	Promethazine VC-Codeine
promethazine/phenylephrine HCl/codeine	promethazine-phenyleph-codeine
pseudoephedrine HCl/acetaminophen	Nexafed Sinus Pressure-Pain
pseudoephedrine HCl/acetaminophen	Sinus HeadacheDegongestant
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Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request

Generic Name	Brand Name	
pseudoephedrine	Allergy Sinus-D	
HCl/acetaminophen/chlorpheniramine		
pseudoephedrine	Non-Aspirin Allergy Sinus	
HCl/acetaminophen/chlorpheniramine		
pseudoephedrine	Non-Aspirin Child's Cold	
HCl/acetaminophen/chlorpheniramine		
pseudoephedrine	Pain Reliever Allergy Sinus	
HCl/acetaminophen/chlorpheniramine		
pseudoephedrine HCl/acrivastine	Semprex-D	
pseudoephedrine HCl/chlophedianol HCl	Rondec-D	
pseudoephedrine HCl/chlophedianol	Certuss-D	
HCI/guaifenesin		
pseudoephedrine HCl/chlophedianol	Vanacof DX	
HCl/guaifenesin		
pseudoephedrine HCl/chlophedianol	Vanatab DX	
HCl/guaifenesin	D AD	
pseudoephedrine HCl/chlorpheniramine	Respa-AR	
maleate/bellad alk	0.1.0	
pseudoephedrine HCI/codeine phosphate	Codar D	
pseudoephedrine HCI/codeine	Maxiflu CD	
phosphate/acetaminophen/guaifen		
pseudoephedrine HCI/codeine	Maxiflu CDX	
phosphate/acetaminophen/guaifen		
pseudoephedrine HCl/codeine	Cheratussin DAC	
phosphate/guaifenesin	Coditionaria DAC	
pseudoephedrine HCl/codeine	Coditussin DAC	
phosphate/guaifenesin	Cuaifanasia DAC	
pseudoephedrine HCl/codeine	Guaifenesin DAC	
phosphate/guaifenesin pseudoephedrine HCl/codeine	Lortuss EX	
phosphate/guaifenesin	LOI LUSS EX	
prosphate/guarrenesin pseudoephedrine HCl/codeine	Phenylhistine	
phosphate/guaifenesin	FIICHYIIISUIIC	
pseudoephedrine HCl/codeine	Tricode GF	
phosphate/guaifenesin	Theode di	
pseudoephedrine HCI/codeine	Tusnel C	
phosphate/guaifenesin	Tushici C	
pseudoephedrine HCl/codeine	Virtussin DAC	
phosphate/guaifenesin	VII COSSIII DAC	
pseudoephedrine HCI/codeine	Zodryl DEC 25	
phosphate/guaifenesin	200.71.020.20	
pseudoephedrine HCI/codeine	Zodryl DEC 30	
phosphate/guaifenesin	200.1.22000	
pseudoephedrine HCI/codeine	Zodryl DEC 35	
phosphate/guaifenesin	1	
pseudoephedrine HCI/codeine	Zodryl DEC 40	
phosphate/guaifenesin	,	
pseudoephedrine HCI/codeine	Zodryl DEC 50	
phosphate/guaifenesin	,	
pseudoephedrine HCI/codeine	Zodryl DEC 60	
pseudoephearme men codeme		

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Generic Name	Brand Name
pseudoephedrine HCl/codeine	Zodryl DEC 80
phosphate/guaifenesin	
pseudoephedrine HCl/codeine/chlorpheniramine	Phenylhistine DH
pseudoephedrine HCl/hydrocodone bitartrate	Rezira
pyrilamine maleate	pyrilamine maleate (bulk)
pyrilamine maleate/chlophedianol HCl	DayClear Allergy Relief
pyrilamine maleate/chlophedianol HCl	Ninjacof
pyrilamine maleate/chlophedianol HCl	VanaCof AC
pyrilamine maleate/chlophedianol HCl	VanaTab AC
pyrilamine maleate/chlophedianol HCl	Vanacof-8
pyrilamine maleate/chlophedianol	Ninjacof-A
HCI/acetaminophen	•
pyrilamine maleate/dextromethorphan HBr	Capron DM
pyrilamine maleate/dextromethorphan HBr	Capron DMT
pyrilamine maleate/phenylephrine	Pro-Chlo
HCI/chlophedianol HCI	
pyrilamine maleate/phenylephrine	Codituss DM
HCI/dextromethorphan HBr	
pyrilamine maleate/pseudoephedrine	Ninjacof-D
HCI/chlophedianol HCI	,
racepinephrine HCl	Asthmanefrin Refill
racepinephrine HCl	Asthmanefrin Starter Kit
racepinephrine HCl	S2 Racepinephrine
racepinephrine HCl	racepinephrine
racepinephrine HCl	racepinephrine (bulk)
reslizumab	Cinqair
revefenacin	Yupelri
roflumilast	Daliresp
salmeterol xinafoate	Serevent Diskus
terbutaline sulfate	terbutaline
theophylline anhydrous	Elixophyllin
theophylline anhydrous	Theo-24
theophylline anhydrous	Theochron
theophylline anhydrous	theophylline
thonzylamine HCl/chlophedianol HCl	POLY HIST PD
thonzylamine HCI/phenylephrine HCI	Nasopen PE
thonzylamine HCl/phenylephrine	Vanacof APE
HCI/chlophedianol HCl	Variation 711 E
thonzylamine HCl/phenylephrine	Poly-Hist DM (thonzylamine)
HCI/dextromethorphan HBr	Toty thist bivi (thonizylanime)
tiotropium bromide	Spiriva Respimat
tiotropium bromide	Spiriva with HandiHaler
tiotropium bromide/olodaterol HCl	Stiolto Respimat
tranilast	tranilast (bulk)
triamcinolone acetonide	24 Hour Nasal Allergy
triamcinolone acetonide	Arze-Ject-A
triamcinolone acetonide	Children's Nasacort
triamcinolone acetonide	
triamcinolone acetonide	Kenalog
	Kenalog-80
triamcinolone acetonide	Nasacort AO
triamcinolone acetonide	Nasacort AQ

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Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request

Generic Name	Brand Name
triamcinolone acetonide	Nasal Allergy
triamcinolone acetonide	P-Care K40
triamcinolone acetonide	P-Care K80
triamcinolone acetonide	Pod-Care 100K
triamcinolone acetonide	Pro-C-Dure 5
triamcinolone acetonide	Pro-C-Dure 6
triamcinolone acetonide	ReadySharp Triamcinolone
triamcinolone acetonide	Zilretta
triamcinolone acetonide	triamcinolone acetonide
triamcinolone acetonide	triamcinolone acetonide (bulk)
triamcinolone acetonide in 0.9 % sodium chloride	triamcinolone aceton-0.9%NaCl
triamcinolone acetonide/0.9% sodium chloride/PF	triamcinol ac (PF) in0.9%NaCl
triamcinolone acetonide/dimethicone	Ellzia Pak
triamcinolone acetonide/dimethicone/silicone,	DermaSilkRx SDS
adhesive	
triamcinolone acetonide/dimethicone/silicone,	DermaWerx SDS
adhesive	
triamcinolone acetonide/dimethicone/silicone,	DermacinRx SilaPak
adhesive	
triamcinolone acetonide/dimethicone/silicone,	NuTriaRx
adhesive	
triamcinolone acetonide/dimethicone/silicone,	SanaDermRx
adhesive	
triamcinolone acetonide/dimethicone/silicone,	Sure Result Tac Pak
adhesive	2
triamcinolone acetonide/dimethicone/silicone,	Tri-Sila
adhesive	53
triamcinolone acetonide/dimethicone/silicone,	Whytederm TDPak
adhesive	,
triamcinolone acetonide/dimethicone/silicone,	Whytederm Trilasil Pak
adhesive	,
triamcinolone acetonide/emollient combination	Pediaderm TA
no.45	
triamcinolone acetonide/emollient combination	Dermasorb TA Complete Kit
no.86	20.masors in complete ne
triamcinolone acetonide/lidocaine HCl	EZ Use Joint-Tunnel-Trigger
triamcinolone acetonide/lidocaine HCl	Lidocilone I
triamcinolone acetonide/lidocaine/prilocaine	DermacinRx Cinlone-I CPI
triamcinolone diacetate in 0.9 % sodium chloride	triamcinolone diacet-0.9%NaCl
triamcinolone diacetate in 0.9 % sodium	triamcinolone diacer-0.9%NaCl
chloride/PF	and monotonical april 1 / 0.3/014aCi
triamcinolone hexacetonide	Aristospan Intra-Articular
triamcinolone hexacetonide	Aristospan Intra-Articular Aristospan Intralesional
triamcinolone hexacetonide	triamcinolone hexaceton(bulk)
triamcinolone hexacetonide, micronized	triamcin hexacet, micro (bulk)
triamcinolone/norflurane and pentafluoropropane	P-Care K40G
(HFC 245fa)	1 Care NTOO
triamcinolone/norflurane and pentafluoropropane	P-Care K80G
(HFC 245fa)	1 Care Rood
triamcinolone/norflurane and pentafluoropropane	Pod-Care 100KG
(HFC 245fa)	I GA-CATE TOOKG
(IIFC 2431d)	

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Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request

Generic Name	Brand Name		
triamcinolone/norflurane and pentafluoropropane	Triloan II SUIK		
(HFC 245fa)			
triamcinolone/norflurane and pentafluoropropane	Triloan SUIK		
(HFC 245fa)			
trimeprazine tartrate	trimeprazine tartrate (bulk)		
tripelennamine HCl	tripelennamine (bulk)		
triprolidine HCl	Histex (triprolidine)		
triprolidine HCl	Histex PD		
triprolidine HCl	Histex PDX		
triprolidine HCl	M-Hist PD		
triprolidine HCl	VanaClear PD		
triprolidine HCl	Vanahist PD		
triprolidine HCl	triprolidine HCl		
triprolidine HCl	triprolidine HCl (bulk)		
triprolidine HCl/phenylephrine HCl/codeine	Histex-AC		
phosphate			
triprolidine HCI/phenylephrine	Histex DM		
HCI/dextromethorphan HBr			
triprolidine HCl/pseudoephedrine HCl	Aprodine		
triprolidine HCI/pseudoephedrine	Trymine CD		
HCI/chlophedianol HCI	,		
umeclidinium bromide	Incruse Ellipta		
umeclidinium bromide/vilanterol trifenatate	Anoro Ellipta		
zafirlukast	Accolate		
zafirlukast	zafirlukast		
zileuton	Zyflo		
zileuton	Zyflo CR		
zileuton	zileuton		
Nonsteroidal Anti-Inf			
CHLORPHENIRAMINE	Advil Allergy-Congestion Rlf		
MALEATE/PHENYLEPHRINE HCL/IBUPROFEN			
CHLORPHENIRAMINE	Advil Allergy Sinus		
MALEATE/PSEUDOEPHEDRINE			
HCL/IBUPROFEN			
HYDROCODONE/IBUPROFEN	Ibudone		
HYDROCODONE/IBUPROFEN	Reprexain		
HYDROCODONE/IBUPROFEN	Vicoprofen		
HYDROCODONE/IBUPROFEN	Xylon 10		
HYDROCODONE/IBUPROFEN	hydrocodone-ibuprofen		
IBUPROFEN	Children's Ibuprofen		
IBUPROFEN	ibuprofen		
IBUPROFEN/OXYCODONE HCL	ibuprofen-oxycodone		
IBUPROFEN/PHENYLEPHRINE HCL	Advil Congestion Relief		
IBUPROFEN/PHENYLEPHRINE HCL	Congestion Relief(ibuprof-PE)		
IBUPROFEN/PSEUDOEPHEDRINE HCL	Advil Cold and Sinus		
IBUPROFEN/PSEUDOEPHEDRINE HCL	Cold and Sinus Pain Relief		
IBUPROFEN/PSEUDOEPHEDRINE HCL	Cold-Sinus Relief		
IBUPROFEN/PSEUDOEPHEDRINE HCL	Ibuprofen Cold		
IBUPROFEN/PSEUDOEPHEDRINE HCL	Ibuprofen Cold-Sinus(withPSE)		
IBUPROFEN/PSEUDOEPHEDRINE HCL	Wal-Profen Cold-Sinus		

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Wal-Profen D Cold and Sinus

IBUPROFEN/PSEUDOEPHEDRINE HCL



Generic Name	Brand Name
INDOMETHACIN	indomethacin
NAPROXEN SODIUM	naproxen sodium
NAPROXEN SODIUM/PSEUDOEPHEDRINE	Aleve Cold and Sinus
HCL	Aleve cold and omas
NAPROXEN SODIUM/PSEUDOEPHEDRINE	Aleve Sinus and Headache
HCL	, neve smas and redudenc
NAPROXEN SODIUM/PSEUDOEPHEDRINE	Aleve-D Sinus and Cold
HCL	2 3 33
NAPROXEN SODIUM/PSEUDOEPHEDRINE	Aleve-D Sinus and Headache
HCL	5 Sinus and nedudone
NAPROXEN SODIUM/PSEUDOEPHEDRINE	All Day Pain Relief Sinus,Cold
HCL	
NAPROXEN SODIUM/PSEUDOEPHEDRINE	Sinus and Cold-D
HCL	
OXAPROZIN	oxaprozin
PIROXICAM	piroxicam
SUMATRIPTAN SUCCINATE/NAPROXEN	Treximet
SODIUM	
celecoxib	Celebrex
celecoxib	celecoxib
diclofenac potassium	Cambia
diclofenac potassium	Cataflam
diclofenac potassium	Zipsor
diclofenac potassium	diclofenac potassium
diclofenac sodium	Voltaren-XR
diclofenac sodium/misoprostol	Arthrotec 50
diclofenac sodium/misoprostol	Arthrotec 75
diclofenac sodium/misoprostol	diclofenac-misoprostol
diclofenac submicronized	Zorvolex
etodolac	Lodine
etodolac	etodolac
fenoprofen calcium	Fenortho
fenoprofen calcium	Nalfon
fenoprofen calcium	ProFeno
fenoprofen calcium	fenoprofen
flurbiprofen	Ansaid
ibuprofen	Advil
ibuprofen	Advil Liqui-Gel
ibuprofen	Advil Migraine
ibuprofen	Child Ibuprofen
ibuprofen	Children's Advil
ibuprofen	Children's Medi-Profen
ibuprofen	Children's Motrin
ibuprofen	Children's Profen IB
ibuprofen	I-Prin
ibuprofen	IBU
ibuprofen	IBU-200
ibuprofen	Ibu-Drops
ibuprofen	Infant's Advil
ibuprofen	Infant's Medi-Profen
ibuprofen	Infant's Motrin

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ibuprofen ibuprofen Motrin IB ibuprofen Motrin IB ibuprofen Provil ibuprofen Provil ibuprofen Provil ibuprofen/diphenhydramine HCl Advil PM Liqui-Gels Advil PM Liqui-Gels ibuprofen/diphenhydramine citrate Motrin PM ibuprofen/diphenhydramine citrate ibuprofen/diphenhydramine citrate ibuprofen/diphenhydramine citrate ibuprofen/diphenhydramine citrate ibuprofen/famotidine Duexis Indomethacin Ind	Generic Name	Brand Name
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	piroxicam	piroxicam
tolmetin sodium tolmetin	sulindac	sulindac
	tolmetin sodium	tolmetin

Diuretics (Thiazides, Potassium Sparing, Loop Diuretics)

amiloride HCl	amiloride
amiloride HCl/hydrochlorothiazide	amiloride-hydrochlorothiazide
bumetanide	bumetanide
chlorothiazide	Diuril
chlorothiazide	chlorothiazide
chlorothiazide sodium	Diuril IV
chlorothiazide sodium	chlorothiazide sodium
chlorthalidone	chlorthalidone
eplerenone	Inspra
eplerenone	eplerenone
ethacrynate sodium	Sodium Edecrin
ethacrynate sodium	ethacrynate sodium
ethacrynic acid	Edecrin
ethacrynic acid	ethacrynic acid
furosemide	Lasix

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Generic Name	Brand Name
furosemide	furosemide
furosemide	furosemide (bulk)
furosemide in 0.9 % sodium chloride	furosemide in 0.9 % NaCl
furosemide/dextrose 5 % in water	furosemide in dextrose 5 %
hydrochlorothiazide	Microzide
hydrochlorothiazide	hydrochlorothiazide
hydrochlorothiazide	hydrochlorothiazide (bulk)
indapamide	indapamide
methyclothiazide	methyclothiazide
metolazone	Zaroxolyn
metolazone	metolazone
spironolactone	Aldactone
spironolactone	CaroSpir
spironolactone	spironolactone
spironolactone	spironolactone (bulk)
spironolactone, micronized	spironolactone micro (bulk)
spironolactone/hydrochlorothiazide	Aldactazide
spironolactone/hydrochlorothiazide	spironolacton-hydrochlorothiaz
torsemide	Demadex
torsemide	torsemide
triamterene	Dyrenium
triamterene	triamterene
triamterene	triamterene (bulk)
triamterene/hydrochlorothiazide	Dyazide
triamterene/hydrochlorothiazide	Maxzide
triamterene/hydrochlorothiazide	Maxzide-25mg
triamterene/hydrochlorothiazide	triamterene-hydrochlorothiazid
trichlormethiazide	trichlormethiazide (bulk)
	Everolimus
everolimus	Afinitor
everolimus	Afinitor Disperz
everolimus	Zortress
	Sirolimus
sirolimus	Rapamune
sirolimus	sirolimus

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Appendix H. Specifications Defining Parameters for this Request

This request executed the Cohort Identification and Descriptive Analysis (CIDA) and Propensity Score Analysis (PSA) modules within the Query Request Package, version 9.7.0, with custom programming to assess the risk for angioedema associated with sacubitril/valsartan (SV) compared to angiotensin-converting enzyme inhibitors (ACEIs) or to angiotensin II receptor blockers (ARBs, excluding SV) among heart failure patients in the Sentinel Distributed Database (SDD).

Query Period: 7/7/2015 - data completeness Coverage Requirement: Medical and drug coverage

Enrollment Requirement: 183 days
Enrollment Gap: 45 days

Age Groups: 18-44, 45-54, 55-64, 65+ years
Output Requested: Attrition table, Kaplan—Meier curves

Additional Programming Needed: Allow SV switchers to re-enter comparisons requiring prior comparator use

by altering PSA pre-processing rules

Notes: Ran against the same ETLs of the SCDM as cder_mpl2r_wp016

		Notes:	Rail agailist the sa	THE LILS OF THE SCD	ivi as cuei_iiipizi_i	wholo		
	Prior comparator use (183 days); angioedema SV users allowed to be in primary exposure group AND comparator					or comparator use ed to be in primary		
		gro	oup			gro	oup	
	Compa	arison 1	Compa	arison 2	Compa	arison 3	Compa	rison 4
Drug/Exposure								
Exposure/Comparator	SV	ACEI	SV	ARBs	SV	ACEI	SV	ARBs
Incident with Respect to:	SV, ARBs	ACEI, ARBs, SV	SV, ACEI	ACEI, ARBs, SV	SV, ARBs	ACEI, ARBs, SV	SV, ACEI	ACEI, ARBs, SV
Incidence Assessment	Dispensing date	e or days supply	Dispensing date	e or days supply	Dispensing dat	e or days supply	Dispensing date	or days supply
Washout (days)	18	83	18	83	1	83	18	33
Cohort Definition	First valid incident	exposure episode	First valid incident	exposure episode	First valid inciden	t exposure episode	First valid incident	exposure episode
Stockpiling Overlapping Claims	Def	ault	Default		Default		Default	
Episode Gap (days)	1	.4	14		14		14	
Episode Extension Period (days)	1	.4	14		1	14	1	4
Maximum Episode Duration (days)	30	65	365		365		365	
Censor Criteria	ACEI	SV	ARBs	SV	ACEI	SV	ARBs	SV
	ARBs, end of treatment, outcome		ACEI, end of treatment, outcome occurrence, disensollment, recorded occurrence, disensollment, recorde		,	,		
	death, dat	a end date	death, data end date		death, data end date		death, data end date	
Inclusion/Exclusion*								
Pre-Existing Condition	Heart failure		Heart failure		Heart failure		Heart failure	
Include/Exclude	Incl	ude	Incl	lude	Include		Incl	ude
Lookback Period (days)	-183, 0		-183, 0		-183, 0		-18	3, 0

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Appendix H. Specifications Defining Parameters for this Request

Appendix H. Specifications Defining P		Prior comparator use (183 days); angioedema				or comparator use	(14 days); angioede	ema	
	SV users allow	SV users allowed to be in primary exposure group AND comparator				ed to be in primary	exposure group A	ND comparator	
		gro	oup			gro	oup		
	Compa	arison 1	Compa	rison 2	Compa	Comparison 3		rison 4	
Pre-Existing Condition	ACEI		ARBs		ACEI		ARBs		
Include/Exclude	Include		Include		Include		Include		
Care Setting/PDX	Any		Any		Any		Any		
Lookback Period (days)	-183, 0		-183, 0		-14, 0		-14, 0		
Inclusion Assessment	Dispensing date		Dispensing date		Dispensing date		Dispensing date		
	or days supply		or days supply		or days supply		or days supply		
Pre-Existing Condition	ACEI, ARBs	SV, ARBs	ARBs, ACEI	SV, ACEI	ACEI, ARBs	SV, ARBs	ARBs, ACEI	SV, ACEI	
Include/Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	
Care Setting/PDX	Any	Any	Any	Any	Any	Any	Any	Any	
Lookback Period	0	0	0	0	0	0	0	0	
Inclusion Assessment	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date	
Event/Outcome									
Event/Outcome	Angio	edema	Angioedema		Angioedema		Angioedema		
Care Setting/PDX	Inpatient, emerge	ncy department or	Inpatient, emergency department or		Inpatient, emergency department or		Inpatient, emerge	ncy department or	
	outp	atient	outpa	atient	outpa	atient	outpa	atient	
Washout (days)		0		0	())	
Blackout Period (days)		0	0		())	
Propensity Score Matching									
Covariates	See Covar_C	ategories tab	See Covar_C	ategories tab	See Covar_C	ategories tab	See Covar_C	ategories tab	
Matching Ratio	1	:1	1:1		1:1		1:1		
Matching Caliper Settings	0.	05	0.05		0.05		0.05		
Analysis Type	Conditional and	d unconditional	Conditional and unconditional		Conditional and unconditional		Conditional and unconditional		
Sensitivity Analysis	PS stratification	stratification with deciles PS stratification with deciles		on with deciles	-				
Subgroup Analyses									
Stratifying variable	Angio	edema	Angioedema		Angioedema		Angioedema		
Evaluation Window (days)	-183	3, -1	-183	3, -1	-183	3, -1	-183	3, -1	
Re-matching	Re-matching sho	Re-matching should be done with		Re-matching should be done with		Re-matching should be done with		Re-matching should be done with	
	the pre-mat	tched cohort	the pre-mat	ched cohort	the pre-mat	ched cohort	the pre-mat	ched cohort	
Stratifying variable	Angio	edema	Angioedema		Angio	edema	Angio	edema	

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Appendix H. Specifications Defining Parameters for this Request

	SV users allowed to be in primary	183 days); angioedema r exposure group AND comparator oup	Prior comparator use (14 days); angioedema SV users allowed to be in primary exposure group AND comparator group		
	Comparison 1	Comparison 2	Comparison 3	Comparison 4	
Evaluation Window (days)	Pre-index enrollment history, -1	Pre-index enrollment history, -1	Pre-index enrollment history, -1	Pre-index enrollment history, -1	
Re-matching	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	
Stratifying variable	Serious allergies	Serious allergies	Serious allergies	Serious allergies	
Evaluation Window (days)	-183, -1	-183, -1		-183, -1	
Re-matching	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	
Stratifying variable	Age group	Age group	Age group	Age group	
Re-matching	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	
Stratifying variable	Sex	Sex	Sex	Sex	
Re-matching	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	
Stratifying variable	Race	Race	Race	Race	
Re-matching	Re-matching should be done with the pre-matched cohort Re-matching should be done with the pre-matched cohort		Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	

^{*} Day 0 EOI/REF dispensing exclusion were not created in input files, but instead achieved by PSA pre-processing.

International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-9/10-CM), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) codes are provided by Optum360. National Drug Codes (NDC) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

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Appendix H. Specifications Defining Parameters for this Request

	Prior comparator use (183 days); angioedema SV users allowed to be in primary exposure group AND comparator group Gap sensitivity analysis				Prior comparator use (183 days); serious angioedema SV users allowed to be in primary exposure group AND comparator group			
	Compa	rison 5	Compa	rison 6	Compa	rison 7	Compa	rison 8
Drug/Exposure								
Exposure/Comparator	SV	ACEI	SV	ARBs	SV	ACEI	SV	ARBs
Incident with Respect to	SV, ARBs	ACEI, ARBs, SV	SV, ACEI	ACEI, ARBs, SV	SV, ARBs	ACEI, ARBs, SV	SV, ACEI	ACEI, ARBs, SV
Incidence Assessment	Dispensing date	or days supply	Dispensing date	or days supply	Dispensing date	e or days supply	Dispensing date	or days supply
Washout (days)	18	33	18	33	18	33	18	33
Cohort Definition	First valid incident	exposure episode	First valid incident	exposure episode	First valid incident	exposure episode	First valid incident	exposure episode
Stockpiling Overlapping Claims	Default		Defa	ault	Def	ault	Def	ault
Episode Gap (days)	,	,	7	7	1	4	1	4
Episode Extension Period (days)	7		7		1	4	14	
Maximum Episode Duration	365		365		365		365	
Censor Criteria	ACEI	SV	ARBs	SV	ACEI	SV	ARBs	SV
	ARBs, end of trea		ACEI, end of trea	tment. outcome	ARBs, end of trea	I atment, outcome	ACEI, end of trea	tment. outcome
	occurrence, disenrollment, recorded		occurrence, disenrollment, recorded				occurrence, disenrollment, recorded	
	death, data	a end date	death, data	a end date	death, dat	a end date	death, dat	a end date
Inclusion/Exclusion*								
Pre-Existing Condition	Heart	failure	Heart	failure	Heart	failure	Heart	failure
Include/Exclude	Incl	ude	Include		Incl	ude	Include	
Lookback Period (days)	-183	3, 0	-183, 0		-18	3, 0	-18	3, 0
Pre-Existing Condition	ACEI		ARBs		ACEI		ARBs	
Include/Exclude	Include		Include		Include		Include	
Care Setting/PDX	Any		Any		Any		Any	
Lookback Period (days)	-183, 0		-183, 0		-183, 0		-183, 0	
Inclusion Assessment	Dispensing date or days supply		Dispensing date or days supply	-	Dispensing date or days supply		Dispensing date or days supply	
Pre-Existing Condition	ACEI, ARBs	SV, ARBs	ARBs, ACEI	SV, ACEI	ACEI, ARBs	SV, ARBs	ARBs, ACEI	SV, ACEI
Include/Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude
Care Setting/PDX	Any	Any	Any	Any	Any	Any	Any	Any
Lookback Period	0	0	0	0	0	0	0	0
Inclusion Assessment	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date	Dispensing date
Event/Outcome								

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Appendix H. Specifications Defining Parameters for this Request

		183 days); angioedema posure group AND comparator group vity analysis	group		
	Comparison 5	Comparison 6	Comparison 7	Comparison 8	
Event/Outcome	Angioedema	Angioedema	Serious Angioedema	Serious Angioedema	
Care Setting/PDX	Inpatient, emergency department or outpatient	Inpatient, emergency department or outpatient	(ED) angioedema diagnosis requiring an intensive care unit admission, intubation, tracheostomy, or	Inpatient or emergency department (ED) angioedema diagnosis requiring an intensive care unit admission, intubation, tracheostomy, or laryngoscopy occurring within 2 days of the date of hospital admission or ED visit	
Washout (days)	0	0	0	0	
Blackout Period (days)	0	0	0	0	
Propensity Score Matching					
Covariates	See Covar_Categories tab	See Covar_Categories tab	See Covar_Categories tab	See Covar_Categories tab	
Matching Ratio	1:1	1:1	1:1	1:1	
Matching Caliper Settings	0.05	0.05	0.05	0.05	
Analysis Type	Conditional and unconditional	Conditional and unconditional	Conditional and unconditional	Conditional and unconditional	
Sensitivity Analysis					
Subgroup Analyses Stratifying variable Evaluation Window (days) Re-matching			Angioedema -183, -1 Re-matching should be done with the pre-matched cohort	Angioedema -183, -1 Re-matching should be done with the pre-matched cohort	
Stratifying variable			Angioedema	Angioedema	
Evaluation Window (days)			Pre-index enrollment history, -1	Pre-index enrollment history, -1	
Re-matching			Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort	

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Appendix H. Specifications Defining Parameters for this Request

	Prior comparator use (183 days); angioedema SV users allowed to be in primary exposure group AND comparator group Gap sensitivity analysis		Prior comparator use (183 SV users allowed to be in primary gro	
	Comparison 5	Comparison 6	Comparison 7	Comparison 8
Stratifying variable			Serious allergies	Serious allergies
Evaluation Window (days)			-183, -1	-183, -1
Re-matching			Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort
Stratifying variable			Age group	Age group
Re-matching			Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort
Stratifying variable			Sex	Sex
Re-matching			Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort
Stratifying variable			Race	Race
Re-matching			Re-matching should be done with the pre-matched cohort	Re-matching should be done with the pre-matched cohort
, , ,	were not created in input files, but instead s, Tenth Revision, Clinical Modification (IC	, , ,	and use Coding System (UCDCS) and C	urrent Dragodural Tarminals - (CDT)

International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-9/10-CM), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) codes are provided by Optum360. National Drug Codes (NDC) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

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Appendix I. Specifications Defining Parameters for Baseline Covariate Groups in this Request

Covariate	Covariate Evaluation Window (days)
Demographic Characteristics	
Age (years, continuous)	Index date
Age-group	
18-44 years*	Index date
45-54 years*	Index date
55-64 years*	Index date
≥65 years*	Index date
Sex	
Male	Index date
Female	Index date
Race/ethnicity	
American Indian or Alaska Native	Index date
Asian	Index date
Black or African American	Index date
Native Hawaiian or Other Pacific Islander	Index date
White	Index date
Unknown	Index date
Year	
2015	Index date
2016	Index date
2017	Index date
2018	Index date
2019	Index date
2020	Index date
Combined Comorbidity Score	
Combined comorbidity score	-183 to 0
Health Conditions	
Angioedema	-183 to -1
Angioedema*	Ever to -1
Ambulatory allergies or allergy treatment*	-183 to -1
Serious allergies (inpatient hospital stays or emergency department visits)	-183 to -1
Ambulatory allergies or treatment and not serious allergies	-183 to -1
Diabetes	-183 to 0
Ischemic heart disease	-183 to 0
Renal disorders	-183 to 0
Medications	
Diuretics (thiazides, potassium sparing, loop diuretics)	-183 to 0
Nonsteroidal anti-inflammatory drugs (NSAIDs)	-183 to 0
Sirolimus	-183 to 0
Everolimus	-183 to 0

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Appendix I. Specifications Defining Parameters for Baseline Covariate Groups in this Request

Covariate	Covariate Evaluation Window (days)
Health care utilization	
Number of inpatient hospital stays	-183 to 0
Number of emergency department visits	-183 to 0
Numer of institutional stay visits	-183 to 0
Number of ambulatory visits	-183 to 0
Number of other ambulatory visits	-183 to 0
Drug utilization	
Number of unique dispensings*	-183 to 0
Number of unique generics dispensed*	-183 to 0
Number of unique drug classes dispensed	-183 to 0

^{*} Covariates followed by an asterisk (*) were not included in the adjusted Propensity Score (PS) model; only those covariates not followed by an asterisk (*) were included in the adjusted PS model.

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