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The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

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_wp032

Request ID: cder_mpl2p_wp032_nsdp_v01

Request Description: In this request, we assessed the risk of angioedema in patients diagnosed with heart failure associated with: 1) sacubitril/valsartan (SV) use comparing those with prior angiotensin-converting enzyme inhibitor (ACEI) use and those with prior angiotensin II receptor blockers (ARBs, not including SV) use; 2) SV use comparing those with and without prior ACEI use; and 3) SV use comparing those with and without prior ARB use. This request is a follow-up analysis to requests cder_mpl2r_wp016_nsdp_v01 and cder_mpl2p_wp021_nsdp_v01.

<u>Sentinel Routine Querying Module:</u> Type 2 Cohort Identification and Descriptive Analysis and Propensity Score (PS) Analysis modules, Query Request Package version 11.2.3, with ad hoc programming

<u>Data Source:</u> The query period spanned from July 7, 2015 through the end of Data Partner (DP)-specific data completeness at the time of execution of prior request, cder_mpl2p_wp021_nsdp_v01. We distributed the analytic package on January 18, 2022. This report contains aggregated data from five DPs which are a subset of the SDD. Data from Medicare patients having both fee-for-service medical coverage and Part D drug coverage are included. The propensity score estimation models converged across comparisons for all DPs. See Appendix A for the list of the query end dates specified for each DP in this query.

<u>Study Design:</u> We identified individuals with incident use of SV who were 18 years or older with a history of heart failure and evaluated occurrence of angioedema during the first qualifying (index) exposure episode. We then conducted pairwise, PS-matched comparisons between SV new users, SV new users with prior ACEI exposure, and SV new users with prior ARB exposure.

Exposure: We defined the exposure of interest using the National Drug Codes (NDCs) recorded in outpatient dispensing data. We defined new use using a 183-day washout period of no prior SV use. For a list of generic and brand names of medical products used to define the exposure drugs, please see Appendix B.

<u>Outcomes of Interest:</u> We defined our 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 outcomes using International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM). For a list of diagnosis codes used to define outcomes, please see Appendix C.

Cohort Eligibility Criteria: We required patients be enrolled in health plans with both medical and drug coverage for at least 183 days before index SV dispensing, during which gaps in coverage of up to 45 days were allowed. The following age groups were included in the cohort: 18-44, 45-54, 55-64 and 65+ years of age. We formed separate cohorts of SV new users, SV new users with ACEI use in the prior 183 days, SV new users with ARB use in the prior 183 days. We also performed sensitivity analyses for SV new users with ACEI use in the prior 14 days and SV new users with ARB use in the prior 14 days. For all SV new user cohorts, we required a diagnosis of heart failure in the 183 days prior to and including index date and no same-day dispensing of ACEI or ARB on the index date. We implemented additional exclusion criterion for each SV new user cohort: SV new users were required to have no ACEI or ARB use in the prior 183 days, SV new users with prior ACEI use were required to have no ARB use in the prior 183 days, and SV new users with prior ARB were required to have no ACEI use in the prior 183 days. Please see Appendix D for a list of generic and brand names of medical products to define inclusion/exclusion criteria in this request. Please see Appendix E for a list of ICD-9-CM and ICD-10-CM diagnosis codes used to define the heart failure inclusion condition for this request.

<u>Follow-up:</u> We determined follow-up time as-treated and based on the length of the exposure episode. We created exposure episodes using days supply recorded in the outpatient pharmacy dispensing data. We bridged together dispensings less than 14 days apart in covered days and added 14 days at the end of each exposure episode to create continuous treatment episodes. 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, including 365 days of continuous SV exposure, and initiation of ACEI or ARB; 3) disenrollment; 4) recorded death; 5) end of exposure episode; or 6) end of query period. Only the first valid exposure episode that occurred during the study period was included per patient.

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Overview for Request: cder_mpl2p_wp032

Baseline Covariates: We summarized the following characteristics for individual SV new user cohorts: demographics as of the index date, including sex, race, Hispanic origin, age, and calendar year; pre-existing conditions or treatment use in the prior 183 days, including ambulatory allergies, ambulatory but not serious allergies, serious allergies, angioedema in the prior 183 days, angioedema throughout the past enrollment history; comorbidities or specific drug utilization in the prior 183 days or on the index date, including combined comorbidity score, diabetes, ischemic heart disease, renal disorders, diuretics, everolimus, nonsteroidal anti-inflammatory drugs, sirolimus; general health services and drug utilization in the prior 183 days or on the index date. Please refer to Appendices F, G, and I for a list of covariates, codes, and evaluation windows used to define characteristics.

<u>Propensity Score Estimation, Matching, and Analysis:</u> For each comparison, we fit a logistic regression model for PS estimation based on potential confounders and risk factors outlined in Appendix I. The matching ratio was 1:1 and the matching caliper was 0.05. Exposure and comparator episodes were nearest neighbor-matched without replacement. For each comparison, we used a risk set-based approach to estimate the hazard ratio and 95% confidence intervals for the site-adjusted analyses, unconditional, and conditional matched analyses. We also estimated period-specific risks separately for 0-30, 31-60, 61-90, 91-180, 181-270, and 271-365 days. Subgroup analyses for effect estimation included angioedema diagnosis in 183 days prior to index date and race.

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 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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- <u>CIDA Glossary</u> List of terms and their definitions found in this report pertaining to Sentinel's Cohort Identification and Descriptive Analysis (CIDA) Tool
- <u>PSA Glossary</u> List of terms and their definitions found in this report pertaining to Sentinel's Propensity Score Analysis (PSA)
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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).

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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.

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.

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



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 metrics to the propensity score estimation model:

- 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

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 included in the "Continuous enrollment before exposure" field.

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 (proportional hazards) regression.

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).

Matching Ratio - patients in exposed and comparator groups are nearest neighbor matched by a 1:1 or 1:n (up to 10) matching ratio.

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 1:1 matched cohort only.

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 patients identified in exposure and comparator cohorts are used in the analysis.

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 returned to the SOC, aggregated, and used to calculate effect estimates.

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 unmatched and the matched population.

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.

*all terms may not be used in this report

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Table 1a. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

(Ondajasted, Aggregated), Fixed Ratio 1:1, et	Medical Product				Covariate Balance		
	ACI	I-SV	AR	B-SV			
					Absolute	Standardized	
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference	
Patients (Number)	68,868	100.0%	48,406	100.0%	-		
		Standard		Standard			
Demographics	Mean	Deviation	Mean	Deviation			
Mean age (years)	70.2	11.2	72.6	10.7	-2.394	-0.218	
Age							
18-44 years	2,374	3.4%	1,136	2.3%	1.100	0.066	
45-54 years	5,060	7.3%	2,588	5.3%	2.001	0.082	
55-64 years	11,290	16.4%	5,863	12.1%	4.282	0.123	
65+ years	50,144	72.8%	38,819	80.2%	<i>-7.383</i>	-0.175	
Sex							
Female	20,972	30.5%	18,939	39.1%	-8.673	-0.183	
Male	47,896	69.5%	29,467	60.9%	8.673	0.183	
Race	227	0.00/	100	2 22/	0.070	0.044	
American Indian or Alaska Native	237	0.3%	129	0.3%	0.078	0.014	
Asian	662	1.0%	1,053	2.2%	-1.214	-0.098	
Black or African American	8,897	12.9%	6,877	14.2%	-1.288	-0.038	
Native Hawaiian or Other Pacific Islander	66	0.1%	59	0.1%	-0.026	-0.008	
Unknown	11,340	16.5%	7,857	16.2%	0.235	0.006	
White	47,666	69.2%	32,431	67.0%	2.216	0.048	
Hispanic Origin	1,336	1.9%	1,123	2.3%	-0.380	-0.026	
Year							
2015	1,336	1.9%	862	1.8%	0.159	0.012	
2016	10,422	15.1%	6,619	13.7%	1.459	0.042	
2017	16,688	24.2%	10,924	22.6%	1.664	0.039	
2018	18,864	27.4%	13,385	27.7%	-0.260	-0.006	
2019	21,239	30.8%	16,324	33.7%	-2.883	-0.062	
2020	319	0.5%	292	0.6%	-0.140	-0.019	
		Standard		Standard			
Recorded History of:	Mean	Deviation	Mean	Deviation			
Charlson/Elixhauser Combined Comorbidity	5.2	2.7	5.4	2.7	-0.156	-0.059	
Score ³							
Ambulatory allergies or allergy treatment	33,387	48.5%	25,738	53.2%	-4.691	-0.094	
Ambulatory allergies or treatment and not	28,086	40.8%	21,351	44.1%	-3.326	-0.067	
serious							
Angioedema (-183, -1)	83	0.1%	56	0.1%	0.005	0.001	
Angioedema (ever, -1)	492	0.7%	740	1.5%	-0.814	-0.077	
Diabetes	34,675	50.3%	25,720	53.1%	-2.784	-0.056	
Ischemic heart disease	54,489	79.1%	37,775	78.0%	1.083	0.026	
Renal disorders	27,082	39.3%	20,921	43.2%	-3.895	-0.079	
Serious allergies	8,036	11.7%	6,440	13.3%	-1.635	-0.049	

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Table 1a. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
	ACE	I-SV	ARB-SV			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	59,667	86.6%	42,247	87.3%	-0.637	-0.019
diuretics)						
Everolimus	11	0.0%	16	0.0%	-0.017	-0.011
Nonsteroidal anti-inflammatory drugs	7,692	11.2%	5,540	11.4%	-0.276	-0.009
(NSAIDs)						
Sirolimus	****	****	****	****	-0.001	-0.001
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.8	13.7	19.2	14.8	-1.364	-0.096
Mean number of emergency room	0.8	1.6	0.7	1.5	0.067	0.043
encounters						
Mean number of inpatient hospital	8.0	1.1	0.8	1.1	0.028	0.026
encounters						
Mean number of non-acute institutional	0.1	0.5	0.1	0.5	0.006	0.012
encounters						
Mean number of other ambulatory	8.2	12.5	8.1	11.9	0.071	0.006
encounters						
Mean number of filled prescriptions	31.2	19.6	32.3	20.8	-1.135	-0.056
Mean number of generics	13.1	5.1	13.8	5.4	-0.692	-0.131
Mean number of unique drug classes	11.4	4.5	12.0	4.7	-0.602	-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 requesterdefined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score pr edicted 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. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, in Risk Assessment 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

(Adjusted, Aggregated), Thed Ratio 1.1, edily	Medical Product				Covariate Balance		
	ACI	EI-SV		B-SV			
					Absolute	Standardized	
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference	
Patients (Number)	46,333	67.3%	46,333	95.7%	-	-	
		Standard		Standard			
Demographics	Mean	Deviation	Mean	Deviation			
Mean age (years)	72.2	10.6	72.2	10.7	-0.039	-0.004	
Age							
18-44 years	1,009	2.2%	1,132	2.4%	-0.265	-0.018	
45-54 years	2,418	5.2%	2,572	5.6%	-0.332	-0.015	
55-64 years	6,571	14.2%	<i>5,796</i>	12.5%	1.673	0.051	
65+ years	36,335	78.4%	36,833	79.5%	-1.075	-0.028	
Sex							
Female	17,309	37.4%	17,308	37.4%	0.002	0.000	
Male	29,024	62.6%	29,025	62.6%	-0.002	-0.000	
Race							
American Indian or Alaska Native	138	0.3%	127	0.3%	0.024	0.004	
Asian	633	1.4%	580	1.3%	0.114	0.010	
Black or African American	6,363	13.7%	6,436	13.9%	-0.158	-0.005	
Native Hawaiian or Other Pacific Islander	59	0.1%	56	0.1%	0.006	0.002	
Unknown	7,557	16.3%	7,528	16.2%	0.063	0.003	
White	31,583	68.2%	31,606	68.2%	-0.050	-0.001	
Hispanic Origin	1,039	2.2%	986	2.1%	0.114	0.008	
Year							
2015	846	1.8%	834	1.8%	0.026	0.002	
2016	6,449	13.9%	6,469	14.0%	-0.043	-0.001	
2017	10,566	22.8%	10,564	22.8%	0.004	0.000	
2018	12,782	27.6%	12,823	27.7%	-0.088	-0.002	
2019	15,424	33.3%	15,370	33.2%	0.117	0.002	
2020	266	0.6%	273	0.6%	-0.015	-0.002	
		Standard		Standard			
Recorded History of:	Mean	Deviation	Mean	Deviation			
Charlson/Elixhauser Combined Comorbidity	5.4	2.7	5.4	2.7	0.010	0.004	
Score ³							
Ambulatory allergies or allergy treatment	24,258	52.4%	24,213	52.3%	0.097	0.002	
Ambulatory allergies or treatment and not	20,229	43.7%	20,146	43.5%	0.179	0.004	
serious							
Angioedema (-183, -1)	55	0.1%	52	0.1%	0.006	0.002	
Angioedema (ever, -1)	340	0.7%	699	1.5%	<i>-0.775</i>	-0.074	
Diabetes	24,321	52.5%	24,306	52.5%	0.032	0.001	
Ischemic heart disease	36,287	78.3%	36,318	78.4%	-0.067	-0.002	
Renal disorders	19,739	42.6%	19,680	42.5%	0.127	0.003	
Serious allergies	6,013	13.0%	6,029	13.0%	-0.035	-0.001	

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Table 1b. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, in Risk Assessment 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			
	ACE	I-SV	ARB-SV			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	40,368	87.1%	40,436	87.3%	-0.147	-0.004
diuretics)						
Everolimus	11	0.0%	12	0.0%	-0.002	-0.001
Nonsteroidal anti-inflammatory drugs	5,241	11.3%	5,186	11.2%	0.119	0.004
(NSAIDs)						
Sirolimus	****	****	****	****	0.002	0.002
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	18.9	14.6	18.8	14.1	0.047	0.003
Mean number of emergency room	0.7	1.4	0.7	1.5	0.011	0.007
encounters						
Mean number of inpatient hospital	0.8	1.1	0.8	1.1	0.004	0.004
encounters						
Mean number of non-acute institutional	0.1	0.5	0.1	0.5	0.000	0.001
encounters						
Mean number of other ambulatory	8.1	11.8	8.1	12.0	0.037	0.003
encounters						
Mean number of filled prescriptions	32.4	20.2	31.7	20.0	0.689	0.034
Mean number of generics	13.6	5.2	13.6	5.2	-0.011	-0.002
Mean number of unique drug classes	11.8	4.6	11.8	4.6	0.023	0.005

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 score pr edicted 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. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database

(SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

(SDD) between July 7, 2015 and February 25,	Medical Product					Covariate Balance		
	ACEI-SV SV							
					Absolute	Standardized		
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference		
Patients (Number)	68,829	100.0%	43,140	100.0%	-	-		
		Standard		Standard				
Demographics	Mean	Deviation	Mean	Deviation				
Mean age (years)	70.2	11.2	71.6	11.9	-1.410	-0.122		
Age								
18-44 years	2,373	3.4%	1,606	3.7%	-0.275	-0.015		
45-54 years	5,058	7.3%	2,977	6.9%	0.448	0.017		
55-64 years	11,281	16.4%	5,949	13.8%	2.600	0.073		
65+ years	50,117	72.8%	32,608	75.6%	-2.773	-0.063		
Sex	20.050	20 50/	45 442	25.00/	F 244	0.444		
Female	20,959	30.5%	15,442	35.8%	-5.344	-0.114		
Male	47,870	69.5%	27,698	64.2%	5.344	0.114		
Race	227	0.20/	120	0.20/	0.022	0.004		
American Indian or Alaska Native	237 664	0.3%	139 531	0.3%		-0.026		
Asian Black or African American		1.0%		1.2%	-0.266			
Native Hawaiian or Other Pacific Islander	8,906 66	12.9% 0.1%	5,806 46	13.5% 0.1%	-0.519 0.011	-0.015 -0.003		
					-0.011			
Unknown	11,333	16.5%	7,114	16.5%	-0.025	-0.001		
White	47,623	69.2%	29,504	68.4%	0.799	0.017		
Hispanic Origin	1,335	1.9%	738	1.7%	0.229	0.017		
Year	1 226	1.9%	420	1.00/	0.047	0.070		
2015	1,336		429	1.0%	0.947	0.079		
2016	10,421	15.1%	4,174	9.7%	5.465	0.166		
2017	16,686	24.2%	9,113	21.1%	3.118	0.075		
2018	18,848	27.4%	12,227	28.3%	-0.959	-0.021		
2019	21,219	30.8%	16,854	39.1%	-8.240	-0.173		
2020	319	0.5% Standard	343	0.8% Standard	-0.332	-0.042		
Described History of	N		0.0					
Recorded History of:	Mean	Deviation	Mean	Deviation	0.200	0.442		
Charlson/Elixhauser Combined Comorbidity	5.2	2.7	5.6	2.8	-0.390	-0.142		
Score ³								
Ambulatory allergies or allergy treatment	33,365	48.5%	21,201	49.1%	-0.669	-0.013		
Ambulatory allergies or treatment and not	28,067	40.8%	17,374	40.3%	0.504	0.010		
serious	0.2	0.40/	50	0.40/	0.046	0.005		
Angioedema (-183, -1)	83	0.1%	59	0.1%	-0.016	-0.005		
Angioedema (ever, -1)	493	0.7%	612	1.4%	-0.702	-0.068		
Diabetes	34,669	50.4%	20,080	46.5%	3.824	0.077		
Ischemic heart disease	54,462	79.1%	32,685	75.8%	3.362	0.080		
Renal disorders	27,064	39.3%	19,253	44.6%	-5.308	-0.108		
Serious allergies	8,028	11.7%	6,019	14.0%	-2.289	-0.069		

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Table 1c. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database

(SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
	ACEI-SV		SV			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	59,637	86.6%	34,664	80.4%	6.293	0.170
diuretics)						
Everolimus	11	0.0%	12	0.0%	-0.012	-0.008
Nonsteroidal anti-inflammatory drugs	7,692	11.2%	4,364	10.1%	1.060	0.034
(NSAIDs)						
Sirolimus	****	****	****	****	-0.012	-0.009
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.8	13.7	18.3	17.3	-0.529	-0.034
Mean number of emergency room	0.8	1.6	0.8	1.6	0.001	0.001
encounters						
Mean number of inpatient hospital	0.8	1.1	0.8	1.1	-0.018	-0.016
encounters						
Mean number of non-acute institutional	0.1	0.5	0.2	0.6	-0.058	-0.104
encounters						
Mean number of other ambulatory	8.2	12.5	9.5	14.5	-1.280	-0.095
encounters						
Mean number of filled prescriptions	31.2	19.7	26.7	20.7	4.477	0.222
Mean number of generics	13.1	5.1	11.7	5.5	1.453	0.273
Mean number of unique drug classes	11.4	4.5	11.0	4.9	0.386	0.082

 $^{^{1}\}mbox{Covariates}$ 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 score pr edicted 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. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment 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

(SDD) between July 7, 2015 and February 29	, 2020 (Aajusi T	ed, Aggregate Medical		te Balance		
	ΔΟΙ	ACEI-SV SV		Covaria	le balance	
	Aci	1			Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	41,518	60.3%	41,518	96.2%	-	-
	, ,	Standard	,	Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	71.6	10.9	71.5	11.8	0.039	0.003
Age						
18-44 years	1,179	2.8%	1,521	3.7%	-0.824	-0.047
45-54 years	2,555	6.2%	2,868	6.9%	-0.754	-0.031
55-64 years	6,074	14.6%	<i>5,737</i>	13.8%	0.812	0.024
65+ years	31,710	76.4%	31,392	75.6%	0.766	0.019
Sex						
Female	14,510	34.9%	14,518	35.0%	-0.019	-0.000
Male	27,008	65.1%	27,000	65.0%	0.019	0.000
Race						
American Indian or Alaska Native	128	0.3%	132	0.3%	-0.010	-0.002
Asian	475	1.1%	482	1.2%	-0.017	-0.002
Black or African American	5,622	13.5%	5,550	13.4%	0.173	0.005
Native Hawaiian or Other Pacific Islander	37	0.1%	40	0.1%	-0.007	-0.002
Unknown	6,641	16.0%	6,668	16.1%	-0.065	-0.003
White	28,615	68.9%	28,646	69.0%	-0.075	-0.002
Hispanic Origin	<i>753</i>	1.8%	708	1.7%	0.108	0.008
Year						
2015	438	1.1%	428	1.0%	0.024	0.002
2016	4,083	9.8%	4,161	10.0%	-0.188	-0.006
2017	8,941	21.5%	9,013	21.7%	-0.173	-0.004
2018	11,903	28.7%	11,895	28.7%	0.019	0.000
2019	15,877	38.2%	15,743	37.9%	0.323	0.007
2020	276	0.7%	278	0.7%	-0.005	-0.001
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.6	2.8	5.6	2.8	-0.005	-0.002
Score ³						
Ambulatory allergies or allergy treatment	20,406	49.1%	20,374	49.1%	0.077	0.002
Ambulatory allergies or treatment and not	16,688	40.2%	16,772	40.4%	-0.202	-0.004
serious	e —					
Angioedema (-183, -1)	47	0.1%	55	0.1%	-0.019	-0.006
Angioedema (ever, -1)	299	0.7%	592	1.4%	-0.706	-0.069
Diabetes	19,584	47.2%	19,531	47.0%	0.128	0.003
Ischemic heart disease	31,745	76.5%	31,755	76.5%	-0.024	-0.001
Renal disorders	18,301	44.1%	18,268	44.0%	0.079	0.002
Serious allergies	5,707	13.7%	5,659	13.6%	0.116	0.003

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Table 1d. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment 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

(355) Seeween July 1, 2013 and 1 estudity 23,	, ,	Medical		te Balance		
	ACEI-SV		SV			
					Absolute	Standardized
Characteristic 1,2	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	34,073	82.1%	34,101	82.1%	-0.067	-0.002
diuretics)						
Everolimus	****	****	****	****	-0.002	-0.002
Nonsteroidal anti-inflammatory drugs	4,302	10.4%	4,273	10.3%	0.070	0.002
(NSAIDs)						
Sirolimus	****	****	****	****	-0.010	-0.009
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	18.1	14.4	18.1	16.8	-0.035	-0.002
Mean number of emergency room	0.8	1.6	0.8	1.6	0.009	0.006
encounters						
Mean number of inpatient hospital	0.8	1.1	0.8	1.1	0.000	0.000
encounters						
Mean number of non-acute institutional	0.2	0.6	0.2	0.6	-0.003	-0.005
encounters						
Mean number of other ambulatory	9.1	13.9	9.1	13.7	-0.041	-0.003
encounters						
Mean number of filled prescriptions	30.1	19.5	27.0	20.7	3.133	0.156
Mean number of generics	12.8	5.1	11.8	5.5	1.044	0.197
Mean number of unique drug classes	11.1	4.5	11.1	4.9	0.019	0.004

 $^{^{1}\}mbox{Covariates}$ 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 score pr edicted 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. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD)

between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

between July 7, 2015 and February 29, 2020	l	Medical	Covariate Balance			
	ΛR	B-SV		SV	Covaria	le Balance
	An				Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	48,455	100.0%	43,845	100.0%	-	-
racients (ramber)	10, 133	Standard	13,013	Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.6	10.7	71.5	11.9	1.087	0.096
Age						
18-44 years	1,136	2.3%	1,651	3.8%	-1.421	-0.083
45-54 years	2,592	5.3%	3,090	7.0%	-1.698	-0.070
55-64 years	5,868	12.1%	6,116	13.9%	-1.839	-0.055
65+ years	38,859	80.2%	<i>32,988</i>	<i>75.2%</i>	4.958	0.119
Sex						
Female	18,947	39.1%	15,531	35.4%	3.680	0.076
Male	29,508	60.9%	28,314	64.6%	-3.680	-0.076
Race						
American Indian or Alaska Native	128	0.3%	144	0.3%	-0.064	-0.012
Asian	1,055	2.2%	525	1.2%	0.980	0.076
Black or African American	6,881	14.2%	5,888	13.4%	0.772	0.022
Native Hawaiian or Other Pacific Islander	59	0.1%	44	0.1%	0.021	0.006
Unknown	7,859	16.2%	7,214	16.5%	-0.234	-0.006
White	32,473	67.0%	30,030	68.5%	-1.474	-0.032
Hispanic Origin	1,128	2.3%	<i>752</i>	1.7%	0.613	0.044
Year						
2015	862	1.8%	429	1.0%	0.801	0.069
2016	6,622	13.7%	4,189	9.6%	4.112	0.129
2017	10,933	22.6%	9,229	21.0%	1.514	0.037
2018	13,394	27.6%	12,481	28.5%	-0.824	-0.018
2019	16,351	33.7%	17,169	39.2%	-5.414	-0.113
2020	293	0.6%	348	0.8%	-0.189	-0.023
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.4	2.7	5.6	2.8	-0.223	-0.082
Score ³						
Ambulatory allergies or allergy treatment	25,740	53.1%	21,467	49.0%	4.160	0.083
Ambulatory allergies or treatment and not	21,353	44.1%	17,616	40.2%	3.890	0.079
serious						
Angioedema (-183, -1)	56	0.1%	59	0.1%	-0.019	-0.005
Angioedema (ever, -1)	738	1.5%	596	1.4%	0.164	0.014
Diabetes	25,762	53.2%	20,413	46.6%	6.610	0.132
Ischemic heart disease	37,818	78.0%	33,251	75.8%	2.210	0.052
Renal disorders	20,953	43.2%	19,524	44.5%	-1.287	-0.026
Serious allergies	6,441	13.3%	6,051	13.8%	-0.508	-0.015

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Table 1e. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD)

between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

Detween July 7, 2013 and 1 colidary 23, 2020 (, ,	Medical		te Balance		
	ARE	3-SV	SV			
					Absolute	Standardized
Characteristic 1,2	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	42,295	87.3%	35,247	80.4%	6.897	0.188
diuretics)						
Everolimus	16	0.0%	12	0.0%	0.006	0.003
Nonsteroidal anti-inflammatory drugs	5,551	11.5%	4,401	10.0%	1.418	0.046
(NSAIDs)						
Sirolimus	****	****	****	****	-0.010	-0.008
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	19.2	14.8	18.3	17.3	0.904	0.056
Mean number of emergency room	0.7	1.5	0.8	1.6	-0.062	-0.041
encounters						
Mean number of inpatient hospital	0.8	1.1	0.8	1.1	-0.042	-0.039
encounters						
Mean number of non-acute institutional	0.1	0.5	0.2	0.6	-0.062	-0.115
encounters						
Mean number of other ambulatory	8.1	11.9	9.4	14.5	-1.305	-0.099
encounters						
Mean number of filled prescriptions	32.4	20.8	26.7	20.7	5.643	0.272
Mean number of generics	13.8	5.4	11.7	5.5	2.162	0.397
Mean number of unique drug classes	12.0	4.7	11.0	4.9	1.005	0.209

 $^{^{1}\}mbox{Covariates}$ 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 score pr edicted 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 1f. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment 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

Number Percent Number Percent Difference Diff	Covariate Balance		
Patients (Number) Absolute Standard Standard Standard Standard Deviation Mean Deviation Deviati	unce		
Patients (Number) Recent Number Percent Number Percent Number Percent Number Percent Difference Di	dardized		
Patients (Number) 37,893 78.2% 37,893 86.4%	ference		
Standard Deviation Devia	-		
Mean age (years) 72.2 10.9 72.3 11.5 -0.033 Age 18-44 years 1,030 2.7% 1,096 2.9% -0.174 -4 45-54 years 2,155 5.7% 2,436 6.4% -0.742 -5 55-64 years 4,701 12.4% 5,046 13.3% -0.910 -6 65+ years 30,007 79.2% 29,315 77.4% 1.826 Sex Female 14,044 37.1% 13,990 36.9% 0.143 Male 23,849 62.9% 23,903 63.1% -0.143 Race American Indian or Alaska Native 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202			
Age 18-44 years 1,030 2.7% 1,096 2.9% -0.174 -45-54 years 2,155 5.7% 2,436 6.4% -0.742 -55-64 years 30,007 79.2% 29,315 77.4% 1.826 Sex Female 14,044 37.1% 13,990 36.9% 0.143 Male 23,849 62.9% 23,903 63.1% -0.143 Race American Indian or Alaska Native 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin Year 2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 2018 10,863 28.7% 10,851 28.6% 0.032 2019 13,870 36.6% 13,991 36.9% -0.019 Standard Recorded History of: Mean Deviation Mean Deviation Mean Deviation Mean Deviation 0.259			
18-44 years	0.003		
45-54 years 2,155 5.7% 2,436 6.4% -0.742 55-64 years 4,701 12.4% 5,046 13.3% -0.910 -65+ years Sex 30,007 79.2% 29,315 77.4% 1.826 Female 14,044 37.1% 13,990 36.9% 0.143 Male 23,849 62.9% 23,903 63.1% -0.143 Race			
55-64 years 4,701 12.4% 5,046 13.3% -0.910 65+ years 30,007 79.2% 29,315 77.4% 1.826 Sex Female 14,044 37.1% 13,990 36.9% 0.143 Male 23,849 62.9% 23,903 63.1% -0.143 Race American Indian or Alaska Native 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin 693 1.8% 691 1.8% 0.005 Year 2015 477 1.3% 418 1.1% 0.156 </td <td>0.011</td>	0.011		
65+ years 30,007 79.2% 29,315 77.4% 1.826 Sex Female 14,044 37.1% 13,990 36.9% 0.143 Male 23,849 62.9% 23,903 63.1% -0.143 Race Ambulatory allergies or allergy treatment 14,044 37.1% 13,990 36.9% 0.143 37.1% 0.143 0.23 0.23 0.31% 0.143 48 0.23,903 63.1% -0.143 0.013 48 0.24 0.50 1.3% 0.103 48 0.16 1.3% 0.103 0.103 49 0.1% 41 0.1% -0.003 41 0.1% -0.003 0.034 41 0.1% -0.003 0.034 41 0.1% -0.003 0.034 41 0.1% -0.034 0.034 41 1.8% 69.1 1.8% 0.005 41 1.9% 4.95 1.8% 0.005 42 2015 477 1.3% 418 1.	0.032		
Sex Female 14,044 37.1% 13,990 36.9% 0.143 Male 23,849 62.9% 23,903 63.1% -0.143 Race Ambulatory allergists or allergy treatment 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin 693 1.8% 691 1.8% 0.005 Year 2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 21.9% 8,331 22.0% -0.095	0.028		
Female Male 14,044 37.1% 13,990 36.9% 0.143 Male 23,849 62.9% 23,903 63.1% -0.143 Race American Indian or Alaska Native 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin 693 1.8% 691 1.8% 0.005 Year 2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 21.9% 8,331 22.0% -0.095 2018 10,863 28.7% 10,851 28.6% 0.032 2	0.048		
Male 23,849 62.9% 23,903 63.1% -0.143 Race American Indian or Alaska Native 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin 693 1.8% 691 1.8% 0.005 Year 2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 21.9% 8,331 22.0% -0.095 2018 10,863 28.7% 10,851 28.6% 0.032 2019 13,870 36.6% 13,991 36.9% -0.319 2020 <td< td=""><td></td></td<>			
Race American Indian or Alaska Native 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin 693 1.8% 691 1.8% 0.005 Year 2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 21.9% 8,331 22.0% -0.095 2018 10,863 28.7% 10,851 28.6% 0.032 2019 13,870 36.6% 13,991 36.9% -0.319 2020 247 0.7% 247 0.7% 0.000 Standard	0.003		
American Indian or Alaska Native 113 0.3% 108 0.3% 0.013 Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin 693 1.8% 691 1.8% 0.005 Year 2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 21.9% 8,331 22.0% -0.095 2018 10,863 28.7% 10,851 28.6% 0.032 2019 13,870 36.6% 13,991 36.9% -0.319 2020 247 0.7% 247 0.7% 0.000 Standard	0.003		
Asian 546 1.4% 507 1.3% 0.103 Black or African American 5,167 13.6% 5,203 13.7% -0.095 Native Hawaiian or Other Pacific Islander 40 0.1% 41 0.1% -0.003 Unknown 5,825 15.4% 5,845 15.4% -0.053 White 26,202 69.1% 26,189 69.1% 0.034 Hispanic Origin 693 1.8% 691 1.8% 0.005 Year 2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 21.9% 8,331 22.0% -0.095 2018 10,863 28.7% 10,851 28.6% 0.032 2019 13,870 36.6% 13,991 36.9% -0.319 2020 247 0.7% 247 0.7% 0.000 Recorded History of: Mean Deviation Mean Deviation Charlson/Elixhauser Combined Comorbidity 5.5 2.7 5.5 2.7 0.009 Score ³ Ambulatory allergies or allergy treatment 19,321 51.0% 19,223 50.7% 0.259			
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2015 477 1.3% 418 1.1% 0.156 2016 4,141 10.9% 4,055 10.7% 0.227 2017 8,295 21.9% 8,331 22.0% -0.095 2018 10,863 28.7% 10,851 28.6% 0.032 2019 13,870 36.6% 13,991 36.9% -0.319 2020 247 0.7% 247 0.7% 0.000 Standard Recorded History of: Mean Deviation Mean Deviation Charlson/Elixhauser Combined Comorbidity 5.5 2.7 5.5 2.7 0.009 Score ³ Ambulatory allergies or allergy treatment 19,321 51.0% 19,223 50.7% 0.259	0.000		
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2019 13,870 36.6% 13,991 36.9% -0.319 2020 247 0.7% 247 0.7% 0.000 Standard Recorded History of: Mean Deviation Mean Deviation Charlson/Elixhauser Combined Comorbidity 5.5 2.7 5.5 2.7 0.009 Score ³ Ambulatory allergies or allergy treatment 19,321 51.0% 19,223 50.7% 0.259	0.002		
2020 247 0.7% 247 0.7% 0.000 Standard Recorded History of: Mean Deviation Mean Deviation Charlson/Elixhauser Combined Comorbidity 5.5 2.7 5.5 2.7 0.009 Score ³ Ambulatory allergies or allergy treatment 19,321 51.0% 19,223 50.7% 0.259	0.001		
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serious			
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	0.007		
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Table 1f. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, in Risk Assessment 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

between July 7, 2013 and 1 est daily 23, 2020 (, ,	Medical	Covariate Balance			
	ARB-SV		SV			
					Absolute	Standardized
Characteristic 1,2	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	32,102	84.7%	32,308	85.3%	-0.544	-0.015
diuretics)						
Everolimus	12	0.0%	11	0.0%	0.003	0.002
Nonsteroidal anti-inflammatory drugs	4,032	10.6%	4,000	10.6%	0.084	0.003
(NSAIDs)						
Sirolimus	****	****	****	****	-0.003	-0.002
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	18.7	14.8	18.7	17.3	0.075	0.005
Mean number of emergency room	0.7	1.6	0.7	1.4	-0.000	-0.000
encounters						
Mean number of inpatient hospital	0.8	1.1	0.8	1.1	0.000	0.000
encounters						
Mean number of non-acute institutional	0.1	0.5	0.1	0.5	0.002	0.004
encounters						
Mean number of other ambulatory	8.5	12.7	8.5	12.4	-0.027	-0.002
encounters						
Mean number of filled prescriptions	30.6	19.7	28.1	20.8	2.476	0.122
Mean number of generics	13.2	5.2	12.1	5.4	1.085	0.205
Mean number of unique drug classes	11.5	4.5	11.5	4.9	0.020	0.004

 $^{^{1}\}mbox{Covariates}$ 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 score pr edicted 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. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

(Olladjusted, Aggregated), Fixed Ratio 1.1, etc.		Medical	Covariate Balance			
	ACEI-S\	ACEI-SV 14-day ARB-SV 14-day				
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	48,920	100.0%	35,084	100.0%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	70.5	11.1	72.8	10.6	-2.333	-0.216
Age						
18-44 years	1,558	3.2%	<i>752</i>	2.1%	1.041	0.065
45-54 years	3,372	6.9%	1,738	5.0%	1.939	0.082
55-64 years	7,879	16.1%	4,166	11.9%	4.232	0.122
65+ years	36,111	73.8%	28,428	81.0%	-7.212	-0.173
Sex						
Female	14,680	30.0%	13,653	38.9%	-8.907	-0.188
Male	34,240	70.0%	21,431	61.1%	8.907	0.188
Race	1.50	0.00/		0.00/	0.000	0.040
American Indian or Alaska Native	160	0.3%	82	0.2%	0.093	0.018
Asian	525	1.1%	847	2.4%	-1.341	-0.103
Black or African American	5,967	12.2%	4,736	13.5%	-1.302	-0.039
Native Hawaiian or Other Pacific Islander	46	0.1%	45	0.1%	-0.034	-0.010
Unknown	7,922	16.2%	5,604	16.0%	0.221	0.006
White	34,300	70.1%	23,770	67.8%	2.363	0.051
Hispanic Origin	973	2.0%	877	2.5%	-0.511	-0.034
Year						
2015	940	1.9%	599	1.7%	0.214	0.016
2016	6,778	13.9%	4,410	12.6%	1.285	0.038
2017	11,541	23.6%	7,696	21.9%	1.656	0.039
2018	13,743	28.1%	9,952	28.4%	-0.273	-0.006
2019	15,681	32.1%	12,211	34.8%	-2.751	-0.058
2020	237	0.5%	216	0.6%	-1.131	-0.018
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.1	2.6	5.3	2.6	-0.196	-0.076
Score ³						
Ambulatory allergies or allergy treatment	23,587	48.2%	18,832	<i>53.7%</i>	-5.461	-0.109
Ambulatory allergies or treatment and not	20,036	41.0%	15,807	45.1%	-4.098	-0.083
serious						
Angioedema (-183, -1)	46	0.1%	33	0.1%	-0.000	-0.000
Angioedema (ever, -1)	330	0.7%	533	1.5%	-0.845	-0.081
Diabetes	24,497	50.1%	18,695	53.3%	-3.211	-0.064
Ischemic heart disease	38,607	78.9%	27,363	78.0%	0.926	0.023
Renal disorders	18,569	38.0%	14,710	41.9%	-3.970	-0.081
Serious allergies	5,343	10.9%	4,442	12.7%	-1.739	-0.054

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Table 1g. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covariate Balance			
	ACEI-SV	/ 14-day	ARB-SV 14-day			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	42,268	86.4%	30,596	87.2%	-0.806	-0.024
diuretics)						
Everolimus	11	0.0%	11	0.0%	-0.009	-0.005
Nonsteroidal anti-inflammatory drugs	5,583	11.4%	4,097	11.7%	-0.265	-0.008
(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	19.0	14.7	-1.493	-0.106
Mean number of emergency room	0.7	1.4	0.7	1.5	0.047	0.032
encounters						
Mean number of inpatient hospital	0.7	1.0	0.7	1.0	0.010	0.009
encounters						
Mean number of non-acute institutional	0.1	0.4	0.1	0.4	0.000	0.000
encounters						
Mean number of other ambulatory	7.3	10.9	7.4	10.6	-0.130	-0.012
encounters						
Mean number of filled prescriptions	31.7	20.1	33.2	21.6	-1.460	-0.070
Mean number of generics	13.2	5.1	14.0	5.4	<i>-0.786</i>	-0.150
Mean number of unique drug classes	11.4	4.5	12.1	4.7	-0.678	-0.147

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 score pr edicted 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. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, in Risk Assessment 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

(Adjusted, Aggregated), Thed Ratio 1.1, edily		Medical	Covariate Balance			
	ACEI-S\	V 14-day		/ 14-day		
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	33,383	68.2%	33,383	95.2%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.4	10.4	72.4	10.5	-0.044	-0.004
Age						
18-44 years	623	1.9%	749	2.2%	-0.377	-0.027
45-54 years	1,679	5.0%	1,723	5.2%	-0.132	-0.006
55-64 years	4,704	14.1%	4,099	12.3%	1.812	0.055
65+ years	26,377	79.0%	26,812	80.3%	-1.303	-0.035
Sex						
Female	12,303	36.9%	12,323	36.9%	-0.060	-0.001
Male	21,080	63.1%	21,060	63.1%	0.060	0.001
Race				/		
American Indian or Alaska Native	85	0.3%	82	0.2%	0.009	0.002
Asian	493	1.5%	471	1.4%	0.066	0.006
Black or African American	4,389	13.1%	4,387	13.1%	0.006	0.000
Native Hawaiian or Other Pacific Islander	37	0.1%	42	0.1%	-0.015	-0.004
Unknown	5,331	16.0%	5,327	16.0%	0.012	0.001
White	23,048	69.0%	23,074	69.1%	-0.078	-0.002
Hispanic Origin	766	2.3%	762	2.3%	0.012	0.001
Year						
2015	576	1.7%	583	1.7%	-0.021	-0.002
2016	4,297	12.9%	4,264	12.8%	0.099	0.003
2017	7,421	22.2%	7,401	22.2%	0.060	0.001
2018	9,432	28.3%	9,499	28.5%	-0.201	-0.004
2019	11,463	34.3%	11,436	34.3%	0.081	0.002
2020	194	0.60%	200	0.60%	-0.018	-0.002
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.2	2.6	5.3	2.6	-0.009	-0.003
Score ³						
Ambulatory allergies or allergy treatment	17,551	52.6%	17,515	52.5%	0.108	0.002
Ambulatory allergies or treatment and not	14,788	44.3%	14,746	44.2%	0.126	0.003
serious						
Angioedema (-183, -1)	25	0.1%	28	0.1%	-0.009	-0.003
Angioedema (ever, -1)	234	0.7%	495	1.5%	-0.782	-0.075
Diabetes	17,520	52.5%	17,515	52.5%	0.015	0.000
Ischemic heart disease	26,098	78.2%	26,160	78.4%	-0.186	-0.005
Renal disorders	13,710	41.1%	13,718	41.1%	-0.024	-0.000
Serious allergies	4,100	12.3%	4,089	12.2%	0.033	0.001

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Table 1h. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, in Risk Assessment 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			
	ACEI-S\	/ 14-day	ARB-SV 14-day			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	29,121	87.2%	29,096	87.2%	0.075	0.002
diuretics)						
Everolimus	****	****	****	****	0.003	0.002
Nonsteroidal anti-inflammatory drugs	3,825	11.5%	3,799	11.4%	0.078	0.002
(NSAIDs)						
Sirolimus	****	****	****	****	-0.006	-0.006
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	18.6	14.4	18.6	13.9	0.013	0.001
Mean number of emergency room	0.7	1.3	0.7	1.5	0.002	0.002
encounters						
Mean number of inpatient hospital	0.7	1.0	0.7	1.0	-0.001	-0.001
encounters						
Mean number of non-acute institutional	0.1	0.4	0.1	0.4	-0.001	-0.003
encounters						
Mean number of other ambulatory	7.4	10.6	7.4	10.7	-0.006	-0.001
encounters						
Mean number of filled prescriptions	33.0	20.9	32.3	20.5	0.665	0.032
Mean number of generics	13.7	5.2	13.7	5.2	-0.037	-0.007
Mean number of unique drug classes	11.9	4.6	11.9	4.6	0.010	0.002

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 score pr edicted 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 1i. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database

(SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

(SDD) between July 7, 2015 and February 29	, zuzu (unad) 	ustea, Aggreg Medical	Covariate Balance				
	ACFI-SV	V 14-day		SV	Covaria	Covariate Dalance	
	ACEIS	laday	•		Absolute	Standardized	
Characteristic 1,2	Number	Percent	Number	Percent	Difference	Difference	
Patients (Number)	48,892	100.0%	44,050	100.0%	-	-	
	-,	Standard	,	Standard			
Demographics	Mean	Deviation	Mean	Deviation			
Mean age (years)	70.5	11.1	71.6	11.9	-1.089	-0.095	
Age							
18-44 years	1,556	3.2%	1,658	3.8%	-0.581	-0.032	
45-54 years	3,372	6.9%	3,056	6.9%	-0.041	-0.002	
55-64 years	7,872	16.1%	6,127	13.9%	2.192	0.061	
65+ years	36,092	73.8%	33,209	75.4%	-1.569	-0.036	
Sex							
Female	14,668	30.0%	15,715	35.7%	-5.675	-0.121	
Male	34,224	70.0%	28,335	64.3%	5.675	0.121	
Race							
American Indian or Alaska Native	160	0.3%	143	0.3%	0.003	0.000	
Asian	525	1.1%	537	1.2%	-0.145	-0.014	
Black or African American	5,969	12.2%	5,968	13.5%	-1.340	-0.040	
Native Hawaiian or Other Pacific Islander	46	0.1%	47	0.1%	-0.013	-0.004	
Unknown	7,919	16.2%	7,229	16.4%	-0.214	-0.006	
White	34,273	70.1%	30,126	68.4%	1.709	0.037	
Hispanic Origin	972	2.0%	<i>758</i>	1.7%	0.267	0.020	
Year							
2015	940	1.9%	429	1.0%	0.949	0.079	
2016	6,778	13.9%	4,188	9.5%	4.356	0.136	
2017	11,538	23.6%	9,252	21.0%	2.596	0.062	
2018	13,734	28.1%	12,543	28.5%	-0.384	-0.009	
2019	15,665	32.0%	17,289	39.2%	-7.209	-0.151	
2020	237	0.5%	349	0.8%	-0.308	-0.039	
		Standard		Standard			
Recorded History of:	Mean	Deviation	Mean	Deviation			
Charlson/Elixhauser Combined Comorbidity	5.1	2.6	5.6	2.8	-0.507	-0.188	
Score ³							
Ambulatory allergies or allergy treatment	23,570	48.2%	21,612	49.1%	-0.854	-0.017	
Ambulatory allergies or treatment and not	20,017	40.9%	17,732	40.3%	0.687	0.014	
serious	ŕ		•				
Angioedema (-183, -1)	46	0.1%	60	0.1%	-0.042	-0.012	
Angioedema (ever, -1)	331	0.7%	621	1.4%	-0.733	-0.072	
Diabetes	24,495	50.1%	20,551	46.7%	3.446	0.069	
Ischemic heart disease	38,588	78.9%	33,377	75.8%	3.154	0.075	
Renal disorders	18,565	38.0%	19,642	44.6%	-6.619	-0.135	
Serious allergies	5,343	10.9%	6,110	13.9%	-2.942	-0.089	
<u>-</u>	•		•				

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Table 1i. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database

(SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

		Medical	Covaria	Covariate Balance		
	ACEI-SV	/ 14-day	sv			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	42,243	86.4%	35,414	80.4%	6.006	0.162
diuretics)						
Everolimus	11	0.0%	12	0.0%	-0.005	-0.003
Nonsteroidal anti-inflammatory drugs	5,584	11.4%	4,435	10.1%	1.353	0.044
(NSAIDs)						
Sirolimus	****	****	****	****	-0.010	-0.008
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.5	13.4	18.3	17.3	-0.805	-0.052
Mean number of emergency room	0.7	1.4	0.8	1.6	-0.053	-0.036
encounters						
Mean number of inpatient hospital	0.7	1.0	0.8	1.1	-0.083	-0.078
encounters						
Mean number of non-acute institutional	0.1	0.4	0.2	0.6	-0.094	-0.184
encounters						
Mean number of other ambulatory	7.3	10.9	9.4	14.5	-2.116	-0.165
encounters						
Mean number of filled prescriptions	31.7	20.1	26.7	20.7	5.044	0.247
Mean number of generics	13.2	5.1	11.7	<i>5.5</i>	1.520	0.287
Mean number of unique drug classes	11.4	4.5	11.0	4.9	0.393	0.084

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 score pr edicted 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 1j. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment 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

(SDD) between July 7, 2015 and February 29		Medical	Covariate Balance			
	ACEI-S\	/ 14-day	SV			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	38,268	78.3%	38,268	86.9%	-	-
		Standard		Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	71.3	10.9	71.3	11.8	-0.010	-0.001
Age						
18-44 years	1,127	2.9%	1,424	3.7%	<i>-0.776</i>	-0.044
45-54 years	2,354	6.2%	2,697	7.0%	-0.896	-0.037
55-64 years	5,729	15.0%	5,416	14.2%	0.818	0.024
65+ years	29,058	75.9%	28,731	75.1%	0.854	0.021
Sex						
Female	12,707	33.2%	12,712	33.2%	-0.013	-0.000
Male	25,561	66.8%	25,556	66.8%	0.013	0.000
Race						
American Indian or Alaska Native	111	0.3%	115	0.3%	-0.010	-0.002
Asian	442	1.2%	453	1.2%	-0.029	-0.003
Black or African American	4,995	13.1%	4,986	13.0%	0.024	0.001
Native Hawaiian or Other Pacific Islander	42	0.1%	40	0.1%	0.005	0.002
Unknown	6,073	15.9%	6,076	15.9%	-0.008	-0.000
White	26,605	69.5%	26,598	69.5%	0.018	0.000
Hispanic Origin	695	1.8%	681	1.8%	0.037	0.003
Year						
2015	424	1.1%	424	1.1%	0.000	0.000
2016	4,000	10.5%	4,026	10.5%	-0.068	-0.002
2017	8,549	22.3%	8,525	22.3%	0.063	0.002
2018	11,112	29.0%	11,080	29.0%	0.084	0.002
2019	13,955	36.5%	13,978	36.5%	-0.060	-0.001
2020	228	0.6%	235	0.6%	-0.018	-0.002
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.3	2.7	5.4	2.6	-0.013	-0.005
Score ³						
Ambulatory allergies or allergy treatment	18,802	49.1%	18,681	48.8%	0.316	0.006
Ambulatory allergies or treatment and not	15,710	41.1%	15,635	40.9%	0.196	0.004
serious						
Angioedema (-183, -1)	42	0.1%	44	0.1%	-0.005	-0.002
Angioedema (ever, -1)	274	0.7%	528	1.4%	-0.664	-0.065
Diabetes	18,299	47.8%	18,298	47.8%	0.003	0.000
Diabetes Ischemic heart disease	18,299 29,508	47.8% 77.1%	18,298 29,592	47.8% 77.3%	0.003 -0.220	0.000 -0.005

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Table 1j. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment 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

(SSS) Secure in July 1, 2013 and 1 estuary 23,		Medical	•	Covariate Balance		
	ACEI-SV	/ 14-day	SV			
					Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	32,038	83.7%	32,112	83.9%	-0.193	-0.005
diuretics)						
Everolimus	****	****	****	****	-0.010	-0.007
Nonsteroidal anti-inflammatory drugs	4,076	10.7%	4,080	10.7%	-0.010	-0.000
(NSAIDs)						
Sirolimus	****	****	****	****	0.000	0.000
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	17.7	13.9	17.8	16.0	-0.026	-0.002
Mean number of emergency room	0.7	1.4	0.7	1.5	0.003	0.002
encounters						
Mean number of inpatient hospital	0.8	1.0	0.8	1.1	-0.001	-0.001
encounters						
Mean number of non-acute institutional	0.1	0.4	0.1	0.4	-0.002	-0.005
encounters						
Mean number of other ambulatory	7.9	11.8	8.0	11.8	-0.063	-0.005
encounters						
Mean number of filled prescriptions	30.9	19.9	27.2	20.5	3.681	0.182
Mean number of generics	12.9	5.0	11.8	5.5	1.105	0.210
Mean number of unique drug classes	11.2	4.4	11.2	4.9	0.005	0.001

 $^{^{1}\}mbox{Covariates}$ 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 score pr edicted 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 1I. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment 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

between July 7, 2015 and February 29, 2020	(Aujusted, Ag	Medical	Covariate Balance			
	ARR-SI	/ 14-day		5V	Covariate Dalance	
	AIND-31	- 14-uay			Absolute	Standardized
Characteristic ^{1,2}	Number	Percent	Number	Percent	Difference	Difference
Patients (Number)	32,174	91.7%	32,174	72.5%	-	-
Tationis (Namber)	32,27 1	Standard	32,17	Standard		
Demographics	Mean	Deviation	Mean	Deviation		
Mean age (years)	72.6	10.6	72.7	11.3	-0.089	-0.008
Age						
18-44 years	<i>735</i>	2.3%	<i>797</i>	2.5%	-0.193	-0.013
45-54 years	1,654	5.1%	1,881	5.8%	-0.706	-0.032
55-64 years	3,887	12.1%	4,200	13.1%	-0.973	-0.030
65+ years	25,898	80.5%	25,296	78.6%	1.871	0.050
Sex						
Female	12,125	37.7%	12,141	37.7%	-0.050	-0.001
Male	20,049	62.3%	20,033	62.3%	0.050	0.001
Race						
American Indian or Alaska Native	80	0.2%	82	0.3%	-0.006	-0.001
Asian	521	1.6%	497	1.5%	0.075	0.006
Black or African American	4,348	13.5%	4,349	13.5%	-0.003	-0.000
Native Hawaiian or Other Pacific Islander	36	0.1%	34	0.1%	0.006	0.002
Unknown	4,900	15.2%	4,860	15.1%	0.124	0.005
White	22,289	69.3%	22,352	69.5%	-0.196	-0.005
Hispanic Origin	695	2.2%	636	2.0%	0.183	0.013
Year						
2015	431	1.3%	402	1.2%	0.090	0.008
2016	3,707	11.5%	3,657	11.4%	0.155	0.005
2017	7,013	21.8%	6,999	21.8%	0.044	0.001
2018	9,266	28.8%	9,270	28.8%	-0.012	-0.000
2019	11,554	35.9%	11,652	36.2%	-0.305	-0.006
2020	203	0.6%	194	0.6%	0.028	0.004
		Standard		Standard		
Recorded History of:	Mean	Deviation	Mean	Deviation		
Charlson/Elixhauser Combined Comorbidity	5.3	2.6	5.3	2.6	-0.002	-0.001
Score ³						
Ambulatory allergies or allergy treatment	16,841	52.3%	16,741	52.0%	0.311	0.006
Ambulatory allergies or treatment and not	14,056	43.7%	14,014	43.6%	0.131	0.003
serious						
Angioedema (-183, -1)	33	0.1%	34	0.1%	-0.003	-0.001
Angioedema (ever, -1)	493	1.5%	457	1.4%	0.112	0.009
Diabetes	16,478	51.2%	16,369	50.9%	0.339	0.007
Ischemic heart disease	24,964	77.6%	24,981	77.6%	-0.053	-0.001
Renal disorders	13,698	42.6%	13,783	42.8%	-0.264	-0.005
Serious allergies	4,136	12.9%	4,154	12.9%	-0.056	-0.002

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Table 1I. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment 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

Detween July 7, 2013 and 1 colidary 23, 2020 (, ,	Medical		Covariate Balance		
	ARB-SV	' 14-day	S	SV		
					Absolute	Standardized
Characteristic 1,2	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	27,771	86.3%	27,925	86.8%	-0.479	-0.014
diuretics)						
Everolimus	****	****	****	****	-0.003	-0.002
Nonsteroidal anti-inflammatory drugs	3,588	11.2%	3,534	11.0%	0.168	0.005
(NSAIDs)						
Sirolimus	****	****	****	****	0.000	0.000
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	18.8	14.6	18.7	17.1	0.048	0.003
Mean number of emergency room	0.7	1.5	0.7	1.4	-0.005	-0.004
encounters						
Mean number of inpatient hospital	0.7	1.0	0.7	1.0	0.001	0.001
encounters						
Mean number of non-acute institutional	0.1	0.4	0.1	0.4	0.002	0.005
encounters						
Mean number of other ambulatory	7.6	10.9	7.5	10.5	0.055	0.005
encounters						
Mean number of filled prescriptions	32.0	20.4	29.0	21.0	2.985	0.144
Mean number of generics	13.6	5.2	12.4	<i>5.4</i>	1.150	0.217
Mean number of unique drug classes	11.7	4.5	11.7	4.8	0.011	0.002

 $^{^{1}\}mbox{Covariates}$ 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 score pr edicted 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. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

between July 7, 2015 and February 25, 2020		Medical	Covariate Balance				
	ARB-S\	/ 14-day		SV	Sovaria		
					Absolute	Standardized	
Characteristic 1,2	Number	Percent	Number	Percent	Difference	Difference	
Patients (Number)	35,088	100.0%	44,361	100.0%	-	-	
		Standard		Standard			
Demographics	Mean	Deviation	Mean	Deviation			
Mean age (years)	72.8	10.5	71.5	11.9	1.286	0.114	
Age							
18-44 years	750	2.1%	1,666	3.8%	-1.618	-0.096	
45-54 years	1,741	5.0%	3,126	7.0%	-2.085	-0.088	
55-64 years	4,166	11.9%	6,193	14.0%	-2.087	-0.062	
65+ years	28,431	81.0%	33,376	75.2%	5.790	0.140	
Sex							
Female	13,649	38.9%	15,727	35.5%	3.447	0.071	
Male	21,439	61.1%	28,634	64.5%	-3.447	-0.071	
Race							
American Indian or Alaska Native	81	0.2%	145	0.3%	-0.096	-0.018	
Asian	847	2.4%	532	1.2%	1.215	0.091	
Black or African American	4,731	13.5%	5,990	13.5%	-0.020	-0.001	
Native Hawaiian or Other Pacific Islander	45	0.1%	46	0.1%	0.025	0.007	
Unknown	5,599	16.0%	7,272	16.4%	-0.436	-0.012	
White	23,785	67.8%	30,376	68.5%	-0.688	-0.015	
Hispanic Origin	879	2.5%	754	1.7%	0.805	0.056	
Year							
2015	599	1.7%	429	1.0%	0.740	0.064	
2016	4,411	12.6%	4,192	9.4%	3.122	0.100	
2017	7,696	21.9%	9,295	21.0%	0.980	0.024	
2018	9,949	28.4%	12,666	28.6%	-0.198	-0.004	
2019	12,217	34.8%	17,427	39.3%	-4.466	-0.093	
2020	216	0.6%	352	0.8%	-0.178	-0.021	
		Standard		Standard			
Recorded History of:	Mean	Deviation	Mean	Deviation			
Charlson/Elixhauser Combined Comorbidity	5.3	2.6	5.6	2.8	-0.307	-0.113	
Score ³							
Ambulatory allergies or allergy treatment	18,821	53.6%	21,702	48.9%	4.718	0.094	
Ambulatory allergies or treatment and not	15,800	45.0%	17,819	40.2%	4.861	0.098	
serious							
Angioedema (-183, -1)	33	0.1%	60	0.1%	-0.041	-0.012	
Angioedema (ever, -1)	533	1.5%	608	1.4%	0.148	0.012	
Diabetes	18,696	53.3%	20,677	46.6%	6.672	0.134	
Ischemic heart disease	27,367	78.0%	33,639	75.8%	2.165	0.051	
Renal disorders	14,714	41.9%	19,754	44.5%	-2.596	-0.052	
Serious allergies	4,439	12.7%	6,108	13.8%	-1.118	-0.033	

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Table 1k. Characteristics of New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, in Risk Assessment of Angioedema in the Sentinel Distributed Database (SDD)

between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05

	Medical Product				Covariate Balance	
	ARB-SV 14-day		SV			
					Absolute	Standardized
Characteristic 1,2	Number	Percent	Number	Percent	Difference	Difference
History of Use:						
Diuretics (thiazides, potassium sparing, loop	30,597	87.2%	35,674	80.4%	6.783	0.185
diuretics)						
Everolimus	11	0.0%	12	0.0%	0.004	0.003
Nonsteroidal anti-inflammatory drugs	4,104	11.7%	4,447	10.0%	1.672	0.054
(NSAIDs)						
Sirolimus	****	****	****	****	-0.008	-0.006
		Standard		Standard		
Health Service Utilization Intensity:	Mean	Deviation	Mean	Deviation		
Mean number of ambulatory encounters	19.0	14.7	18.3	17.3	0.710	0.044
Mean number of emergency room	0.7	1.5	0.8	1.6	-0.099	-0.065
encounters						
Mean number of inpatient hospital	0.7	1.0	0.8	1.1	-0.091	-0.085
encounters						
Mean number of non-acute institutional	0.1	0.4	0.2	0.6	-0.093	-0.184
encounters						
Mean number of other ambulatory	7.4	10.6	9.4	14.4	-1.958	-0.154
encounters						
Mean number of filled prescriptions	33.2	21.6	26.7	20.7	6.520	0.308
Mean number of generics	14.0	5.4	11.6	5.5	2.314	0.425
Mean number of unique drug classes	12.1	4.7	11.0	4.9	1.079	0.224

 $^{^{1}\}mbox{Covariates}$ 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 score pr edicted 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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

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) ¹	Wald P-Value ¹
						Overall					
Site-Adjusted Analys	sis										
ACEI-SV	68,868	****	****	****	****	2.15	****	-0.47	****	0.83 (0.55, 1.24)	0.356
ARB-SV	48,406	****	****	****	****	2.62	****	-0.47		0.83 (0.33, 1.24)	0.330
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	46,333	****	****	****	****	2.74	****	-0.37	****	0.00 / 0.50 1.56)	0.662
ARB-SV	46,333	****	****	****	****	3.11	****	-0.37		0.88 (0.50, 1.56)	0.662
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	46,333	****	****	****	****	2.11	****	-0.49	****	0.01/0.53 1.30)	0.360
ARB-SV	46,333	****	****	****	****	2.6	****	-0.49		0.81 (0.52, 1.28)	0.369
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV	68,868	****	****	****	****	3.5	****	-0.38	****	0.91 (0.45, 1.82)	0.784
ARB-SV	48,406	****	****	****	****	3.89	****	-0.56		0.91 (0.45, 1.62)	0.764
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	46,333	****	****	****	****	4.46	****	0.22	****	4.00 (0.54 - 2.20)	0.047
ARB-SV	46,333	****	****	****	****	4.14	****	0.32	4.4.4.4.4	1.08 (0.51, 2.29)	0.847
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	46,333	****	****	****	****	4.64	****	0.00	****	1 22 / 0 50 2 56)	0.575
ARB-SV	46,333	****	****	****	****	3.76	****	0.88	and the state of	1.23 (0.59, 2.56)	0.575
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV	55,636	****	****	****	****	3.18	****	0.15	****	1.06 (0.42 2.50)	0.004
ARB-SV	38,892	****	****	****	****	3.02	****	0.15	ran ran ran ran	1.06 (0.43, 2.59)	0.904

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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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in	Hannad Badia	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	30,021	****	****	****	****	2.88	****	-1.15	****	0.71 (0.23, 2.25)	0.566
ARB-SV	30,021	****	****	****	****	4.03	****	-1.15		0.71 (0.23, 2.23)	0.300
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	37,183	****	****	****	****	2.37	****	-0.77	****	0.76 (0.26, 2.18)	0.604
ARB-SV	37,346	****	****	****	****	3.15	****	-0.77		0.76 (0.26, 2.16)	0.604
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV	37,553	****	****	****	****	2.5	****	-1.07	****	0.68 (0.24, 1.95)	0.477
ARB-SV	26,335	****	****	****	****	3.57	****	-1.07		0.08 (0.24, 1.93)	0.477
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	13,807	****	****	****	****	2.13	****	4.07	****	0.67 (0.44 . 2.00)	0.657
ARB-SV	13,807	****	****	****	****	3.2	****	-1.07	****	0.67 (0.11, 3.99)	0.657
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	25,121	****	****	****	****	1.61	****	2.11	****	0.43 / 0.44 - 1.66	0.210
ARB-SV	25,311	****	****	****	****	3.71	****	-2.11		0.43 (0.11, 1.66)	0.219
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV	30,181	****	****	****	****	0.52	****	-1.72	****	0.23 (0.06, 0.87)	0.029
ARB-SV	21,257	****	****	****	****	2.25	****	-1.72		0.23 (0.06, 0.87)	0.029
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	8,985	****	****	****	****	0.75	****		****		_
ARB-SV	8,985	****	****	****	****	0.75	****	0	****	1.00 (0.06, 15.99)	1
Fixed Ratio 1:1 Prop	· · · · · · · · · · · · · · · · · · ·	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	20,130	****	****	****	****	0.79	****	4.55	****	0.24 / 0.00 . 4.24)	0.404
ARB-SV	20,464	****	****	****	****	2.33	****	-1.55	***	0.34 (0.09, 1.24)	0.101
	· ·				181	- 270 Days					
Site-Adjusted Analys	sis										
ACEI-SV	18,797	****	****	****	****	1.82	****	0.2	****	4.24 / 0.26 . 4.22\	0.724
ARB-SV	13,036	****	****	****	****	1.51	****	0.3	7-7-7-7-	1.24 (0.36, 4.23)	0.734

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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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	3,442	****	****	****	****	0	****	1 72	****		
ARB-SV	3,442	****	****	****	****	1.72	****	-1.72	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	12,497	****	****	****	****	1.57	****	0	****	1.01/0.25 4.02\	0.002
ARB-SV	12,557	****	****	****	****	1.57	****	0		1.01 (0.25, 4.03)	0.992
					271	- 365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	13,147	****	****	****	****	1.72	****	0.7	****	1 71 / 0 22 0 01)	0.533
ARB-SV	8,956	****	****	****	****	1.03	****	0.7		1.71 (0.33, 8.81)	0.522
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	1,630	****	****	****	****	0	****	0	****		
ARB-SV	1,630	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	8,598	****	****	****	****	1.06	****	0.52	****	2 02 / 0 19 22 22\	0.565
ARB-SV	8,641	****	****	****	****	0.53	****	0.53		2.02 (0.18, 22.33)	0.565
1				•			_				

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, 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 Risk Window

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) ¹	Wald P-Value ¹
No Angioedema (-18	33, -1)										
						Overall					
Site-Adjusted Analys											
ACEI-SV	68,785	****	****	****	****	2.07	****	-0.2	****	0.92 (0.61, 1.41)	0.71
ARB-SV	48,350	****	****	****	****	2.26	****				
Fixed Ratio 1:1 Prop		tched Cond	ditional Ana								
ACEI-SV	46,272	****	****	****	****	2.61	****	0	****	1.00 (0.55, 1.83)	1
ARB-SV	46,272	****	****	****	****	2.61	****	0		1.00 (0.55, 1.65)	
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cal	iper= 0.05						
ACEI-SV	46,272	****	****	****	****	2.05	****	-0.24	****	0.90 (0.56, 1.43)	0.649
ARB-SV	46,272	****	****	****	****	2.29	****	-0.24		0.90 (0.30, 1.43)	0.049
					0	- 30 Days					
Site-Adjusted Analys											
ACEI-SV	68,785	****	****	****	****	3.31	****	0.81	****	1.33 (0.59, 2.98)	0.49
ARB-SV	48,350	****	****	****	****	2.5	****	0.81		1.33 (0.39, 2.98)	0.49
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	46,272	****	****	****	****	4.14	****	1 20	****	1 44 (0 62 - 2 20)	0.396
ARB-SV	46,272	****	****	****	****	2.87	****	1.28		1.44 (0.62, 3.38)	0.396
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	46,272	****	****	****	****	4.36	****	1.75	****	1 67 (0 72 2 92)	0.224
ARB-SV	46,272	****	****	****	****	2.61	****	1./5		1.67 (0.73, 3.82)	0.224
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV	55,566	****	****	****	****	2.91	****	-0.11	****	0.97 (0.39, 2.41)	0.944
ARB-SV	38,851	****	****	****	****	3.03	****	-0.11		0.37 (0.33, 2.41)	0.344

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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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, 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 Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop						Tears	New Oscis	icais	itew oscis	intervary	1 Value
ACEI-SV	29,989	****	****	*****	****	2.88	****				
ARB-SV	29,989	****	****	****	****	4.03	****	-1.15	****	0.71 (0.23, 2.25)	0.566
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalysis: Cali	iper= 0.05	4.03					
ACEI-SV	37,131	****	****	****	****	2.38	****				
ARB-SV	37,302	****	****	****	****	3.15	****	-0.77	****	0.76 (0.26, 2.18)	0.604
	5.,65=				61	- 90 Days					
Site-Adjusted Analys	sis					•					
ACEI-SV	37,510	****	****	****	****	2.51	****	0.56	****	0.01 (0.07 2.42)	0.711
ARB-SV	26,307	****	****	****	****	3.07	****	-0.56		0.81 (0.27, 2.42)	0.711
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	13,790	****	****	****	****	2.13	****	4.07	****	0.67 (0.44 . 2.00)	0.657
ARB-SV	13,790	****	****	****	****	3.2	****	-1.07	****	0.67 (0.11, 3.99)	0.657
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	25,090	****	****	****	****	1.61	****	-1.58	****	0.50 (0.13, 2.02)	0.333
ARB-SV	25,283	****	****	****	****	3.19	****	-1.56		0.50 (0.15, 2.02)	0.555
					91	- 180 Days					
Site-Adjusted Analys											
ACEI-SV	30,151	****	****	****	****	0.52	****	-1.73	****	0.23 (0.06, 0.86)	0.029
ARB-SV	21,233	****	****	****	****	2.25	****	-1.75		0.23 (0.00, 0.00)	0.023
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	8,981	****	****	****	****	0.75	****	0	****	1.00 (0.06, 15.99)	1
ARB-SV	8,981	****	****	****	****	0.75	****			1.00 (0.00, 13.99)	
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV	20,107	****	****	****	****	0.79	****	-1.55	****	0.34 (0.09, 1.24)	0.101
ARB-SV	20,440	****	****	****	****	2.34	****	-1.55		0.54 (0.05, 1.24)	0.101

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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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years		Years	of	Person	•	Person	1.000	(95% Confidence	Wald
			Days				1,000		,	•	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Site-Adjusted Analy	voic				181	270 Days					
ACEI-SV	18,775	****	****	****	****	1.82	****				
ARB-SV	13,024	****	****	****	****	1.52	****	0.3	****	1.24 (0.36, 4.23)	0.734
		tabad Cam	d:4: 1 A	husia. Calina	0 0F ²	1.52					
Fixed Ratio 1:1 Prop		****	****	****	*****	0	****				
ACEI-SV ARB-SV	3,442	****	****	****	****	1.72	****	-1.72	****	-	-
Fixed Ratio 1:1 Prop	3,442					1.72					
ACEI-SV	12,481	****	****	****	*****	1.57	****				
ARB-SV	12,544	****	****	****	****	1.57	****	0	****	1.01 (0.25, 4.02)	0.993
AILD-3V	12,344				271	L - 365 Days					
Site-Adjusted Analy	sis					. 303 Days					
ACEI-SV	13,130	****	****	****	****	1.72	****				
ARB-SV	8,947	****	****	****	****	1.03	****	0.7	****	1.71 (0.33, 8.81)	0.522
Fixed Ratio 1:1 Prop		tched Cond	ditional Ana	lysis: Caline	r= 0.05 ²						
ACEI-SV	1,631	****	****	****	****	0	****				
ARB-SV	1,631	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Unc	onditional A	nalvsis: Cal	iper= 0.05						
ACEI-SV	8,587	****	****	****	****	1.06	0.23		****		
ARB-SV	8,632	****	****	****	****	0.53	0.12	0.53	****	2.02 (0.18, 22.31)	0.565
Angioedema (-183,											
						Overall					
Site-Adjusted Analy	sis										
ACEI-SV	83	****	****	****	****	72.23	****	261.11	****	0.26 / 0.05 1.22\	0.105
ARB-SV	56	****	****	****	****	333.33	****	-261.11		0.26 (0.05, 1.33)	0.105

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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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	46	****	****	****	****	164.47	****	-328.95	****	0.33 (0.03, 3.20)	0.341
ARB-SV	46	****	****	****	****	493.42	****	-526.95		0.33 (0.03, 3.20)	0.541
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	46	****	****	****	****	64.77	****	-143.57	****	0.31 (0.03, 2.96)	0.308
ARB-SV	46	****	****	****	****	208.33	****	-143.57		0.31 (0.03, 2.30)	0.308
					0	- 30 Days					
Site-Adjusted Analys											
ACEI-SV	83	****	****	****	****	156.99	****	-1089.9	****	0.13 (0.02, 1.11)	0.063
ARB-SV	56	****	****	****	****	1,246.88	****	1003.5		0.15 (0.02, 1.11)	0.005
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	46	****	****	****	****	332.23	****	-664.45	****	0.33 (0.03, 3.20)	0.341
ARB-SV	46	****	****	****	****	996.68	****	-004.43		0.33 (0.03, 3.20)	0.341
Fixed Ratio 1:1 Prope	ensity Score Ma				•						
ACEI-SV	46	****	****	****	****	285.71	****	-628.92	****	0.31 (0.03, 2.96)	0.308
ARB-SV	46	****	****	****	****	914.63	****	-028.92		0.31 (0.03, 2.90)	0.308
					31	- 60 Days					
Site-Adjusted Analys											
ACEI-SV	73	****	****	****	****	204.92	****	204.92	****	_	_
ARB-SV	45	****	****	****	****	0	****	204.32			_
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	31	****	****	****	****	0	****	0	****		
ARB-SV	31	****	****	****	****	0	****	0	ren ren ren ren	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	40	****	****	****	****	0	****	0	****		
ARB-SV	36	****	****	****	****	0	****	U		-	-

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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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1.000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days				,	
Site-Adjusted Analy	sis										
ACEI-SV	47	****	****	****	****	0	****	-432.9	****		
ARB-SV	30	****	****	****	****	432.9	****	-432.9		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	17	****	****	****	****	0	****	0	****		
ARB-SV	17	****	****	****	****	0	****	0	de de de de de	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	27	****	****	****	****	0	****	0	****		
ARB-SV	25	****	****	****	****	0	****	U		-	
					91	- 180 Days					
Site-Adjusted Analy	sis										
ACEI-SV	33	****	****	****	****	0	****	0	****		
ARB-SV	26	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	11	****	****	****	****	0	****	0	****		
ARB-SV	11	****	****	****	****	0	****	0	7777	-	<u>-</u>
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	21	****	****	****	****	0	****	0	****		
ARB-SV	21	****	****	****	****	0	****	U		-	
					181	- 270 Days					
Site-Adjusted Analy	sis										
ACEI-SV	23	****	****	****	****	0	****	0	****		
ARB-SV	15	****	****	****	****	0	****	U		-	_

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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 New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, 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 Risk Window

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	Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV ARB-SV	****	*****	*****	****	*****	0 0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV ARB-SV	14 12	*****	***** ****	****	*****	0	****	0	****	-	-
					271	- 365 Days					
Site-Adjusted Analys	sis										
ACEI-SV ARB-SV	18 13	*****	****	****	****	0 0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****	0	****		
ARB-SV	****	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV ARB-SV	****	****	****	*****	*****	0 0	****	0	****	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Race: Unknown						Overall					
Site-Adjusted Analy	eic					Overall					
ACEI-SV	11,340	****	****	****	****	1.28	****				
ARB-SV	7.857	****	****	****	****	1.51	****	-0.22	****	0.79 (0.21, 2.94)	0.723
Fixed Ratio 1:1 Prop	,	tched Cone	ditional Ana	lycic: Calina	r- 0.05 ²	1.51					
ACEI-SV	7,448	****	****	****	*****	0.81	****				
ARB-SV	7,448 7,448	****	****	****	****	1.62	****	-0.81	****	0.50 (0.05, 5.51)	0.571
Fixed Ratio 1:1 Prop		tched Unco	nnditional A	nalvsis: Cal	iner= 0 05	1.02					
ACEI-SV	7,448	****	****	****	****	1.2	****				
ARB-SV	7,448	****	****	****	****	1.58	****	-0.38	****	0.73 (0.16, 3.28)	0.686
AIRE SV	7,440				0	- 30 Days					
Site-Adjusted Analy	rsis										
ACEI-SV	11,340	****	****	****	****	1.21	****		****		
ARB-SV	7,857	****	****	****	****	3.5	****	-2.29	****	0.34 (0.03, 3.75)	0.376
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Calipe	r= 0.05 ²						
ACEI-SV	7,448	****	****	****	****	0	****		****		
ARB-SV	7,448	****	****	****	****	4.12	****	-4.12	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	7,448	****	****	****	****	1.85	****	4.02	****	0.50/0.05 5.53)	0.572
ARB-SV	7,448	****	****	****	****	3.68	****	-1.83	nan nan nan nan	0.50 (0.05, 5.52)	0.572
					31	- 60 Days					
Site-Adjusted Analy	sis										
ACEI-SV	8,766	****	****	****	****	3.32	****	3.32	****		
ARB-SV	6,039	****	****	****	****	0	****	3.32		-	-

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop						1 Cai 3	ivew osers	i cais	New Osers	intervary	r-value
ACEI-SV	4,446	****	*****	****	****	3.84	****				
ARB-SV	4,446 4,446	****	****	****	****	0	****	3.84	****	-	-
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalysis: Cali	iner- 0 05	<u> </u>					
ACEI-SV	5,703	****	*****	*****	****	2.56	****				
ARB-SV	5,703 5,747	****	****	****	****	2.50	****	2.56	****	-	-
AILD-3V	3,747				61	- 90 Days					
Site-Adjusted Analys	sis					56 24 76					
ACEI-SV	6,045	****	****	****	****	2.23	****		ate ate ate ate		
ARB-SV	4,105	****	****	****	****	3.29	****	-1.05	****	0.59 (0.04, 9.43)	0.708
Fixed Ratio 1:1 Prop		tched Cond	ditional Ana	lysis: Calipe	r= 0.05 ²						
ACEI-SV	2,097	****	****	****	****	0	****				
ARB-SV	2.097	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	,	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV	3,919	****	****	****	****	0	****		****		
ARB-SV	3,904	****	****	****	****	3.45	****	-3.45	****	-	-
	,				91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV	4,821	****	****	****	****	0	****	4.55	****		
ARB-SV	3,286	****	****	****	****	1.57	****	-1.57	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	1,344	****	****	****	****	0	****		****		
ARB-SV	1,344	****	****	****	****	0	****	0	***	-	-
Fixed Ratio 1:1 Prop		tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV	3,119	****	****	****	****	0	****	1.64	****		
	3,135	****	****	****	****	1.64	****	-1.64	4-4-4-4-4-	-	-

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
	Hell Coels	ut mon	ut mon	GC THISIC		270 Days	Hell Cocio		iteli oseis	ter var,	
Site-Adjusted Analy	sis					,					
ACEI-SV	3,040	****	****	****	****	0	****		****		
ARB-SV	2,080	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Con	ditional Ana	lvsis: Calipe	er= 0.05 ²						
ACEI-SV	552	****	****	****	****	0	****	_	****		
ARB-SV	552	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	1,935	****	****	****	****	0	****		****		
ARB-SV	1,991	****	****	****	****	0	****	0	****	-	-
	·				271	365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	2,130	****	****	****	****	2.13	****	2.12	****		
ARB-SV	1,422	****	****	****	****	0	****	2.13		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	249	****	****	****	****	0	****		****		
ARB-SV	249	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	1,333	****	****	****	****	3.45	****	2.45	****		
ARB-SV	1,364	****	****	****	****	0	****	3.45		-	-
Race: American Ind	ian										
						Overall					
Site-Adjusted Analy											
ACEI-SV	237	****	****	****	****	0	****	0	****		
ARB-SV	129	****	****	****	****	0	****	U		-	_

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	119	****	****	****	****	0	****	0	****		
ARB-SV	119	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	119	****	****	****	****	0	****	0	****		
ARB-SV	119	****	****	****	****	0	****	U		-	-
					0	- 30 Days					
Site-Adjusted Analys											
ACEI-SV	237	****	****	****	****	0	****	0	****	_	_
ARB-SV	129	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	119	****	****	****	****	0	****	0	****		
ARB-SV	119	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	119	****	****	****	****	0	****	0	****		
ARB-SV	119	****	****	****	****	0	****	0		-	-
					31	- 60 Days					
Site-Adjusted Analys											
ACEI-SV	189	****	****	****	****	0	****	0	****		
ARB-SV	101	****	****	****	****	0	****	0			_
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	70	****	****	****	****	0	****	0	****		
ARB-SV	70	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	86	****	****	****	****	0	****	0	****		
ARB-SV	93	****	****	****	****	0	****	U		-	-

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

		Daman	Average	Average	Normalian	Incidence Rate per	Dial. man	Incidence Rate Difference	Difference in	Hazard Ratio	
	Number of	Person Years	Person Days	Person Years	Number of	1,000 Person	Risk per 1,000	per 1,000 Person	Risk per 1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Wiedical Froduct	New Osers	αι ινιον	αι Νίοκ	at Nisk		- 90 Days	New Osers	rears	New Osers	intervarj	r-value
Site-Adjusted Analy	rsis					30 24,5					
ACEI-SV	121	****	****	****	****	0	****		ale ale ale ale		
ARB-SV	64	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	27	****	****	****	****	0	****		****		
ARB-SV	27	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	56	****	****	****	****	0	****	0	****	_	
ARB-SV	60	****	****	****	****	0	****	U		-	
					91	- 180 Days					
Site-Adjusted Analy											
ACEI-SV	98	****	****	****	****	0	****	0	****	_	_
ARB-SV	56	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	19	****	****	****	****	0	****	0	****		
ARB-SV	19	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cal	-						
ACEI-SV	44	****	****	****	****	0	****	0	****	_	_
ARB-SV	53	****	****	****	****	0	****				
					181	- 270 Days					
Site-Adjusted Analy											
ACEI-SV	56	****	****	****	****	0	****	0	****	-	_
ARB-SV	33	****	****	****	****	0	****	•			

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****		****		
ARB-SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	24	****	****	****	****	0	****	0	****		
ARB-SV	32	****	****	****	****	0	****	0		-	-
					271	- 365 Days					
Site-Adjusted Analysi	is										
ACEI-SV	39	****	****	****	****	0	****	0	****		
ARB-SV	19	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****	0	****		
ARB-SV	****	****	****	****	****	0	****	0	de de de de de	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	18	****	****	****	****	0	****	0	****		
ARB-SV	20	****	****	****	****	0	****	U		-	
Race: Asian											
						Overall					
Site-Adjusted Analys	is										
ACEI-SV	662	****	****	****	****	0	****	2.02	****		
ARB-SV	1,053	****	****	****	****	2.93	****	-2.93		-	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	569	****	****	****	****	0	****	0	****		
ARB-SV	569	****	****	****	****	0	****	0	ren ren ren ren	-	-

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	569	****	****	****	****	0	****		****		
ARB-SV	569	****	****	****	****	5.17	****	-5.17	****	-	-
					0 -	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV	662	****	****	****	****	0	****	0	****		
ARB-SV	1,053	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	569	****	****	****	****	0	****	0	****		
ARB-SV	569	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	569	****	****	****	****	0	****	0	****		
ARB-SV	569	****	****	****	****	0	****	U		-	
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV	509	****	****	****	****	0	****	0	****	_	_
ARB-SV	774	****	****	****	****	0	****				_
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	336	****	****	****	****	0	****	0	****		
ARB-SV	336	****	****	****	****	0	****	0		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Mat				•						
ACEI-SV	442	****	****	****	****	0	****	0	****	_	_
ARB-SV	434	****	****	****	****	0	****	U		-	-

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

		Person	Average Person	Average Person	Number	Incidence Rate per 1,000	Risk per	Incidence Rate Difference per 1,000	Difference in Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV	351	****	****	****	****	0	****	0	****	_	_
ARB-SV	515	****	****	****	****	0	****	0			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	163	****	****	****	****	0	****	0	****		
ARB-SV	163	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	303	****	****	****	****	0	****	0	****		
ARB-SV	293	****	****	****	****	0	****	U		-	-
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV	267	****	****	****	****	0	****	0	****		
ARB-SV	411	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	99	****	****	****	****	0	****		****		
ARB-SV	99	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	231	****	****	****	****	0	****	0	****		
ARB-SV	234	****	****	****	****	0	****	0	71 71 71 71	-	-
					181	- 270 Days					
Site-Adjusted Analy	sis										
ACEI-SV	178	****	****	****	****	0	****	-18.22	****		
ARB-SV	271	****	****	****	****	18.22	****	-10.22		-	-

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Proper	nsity Score Mat	ched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	43	****	****	****	****	0	****		****		
ARB-SV	43	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Proper	nsity Score Mat	ched Unco	nditional A	nalysis; Cali	per= 0.05						
ACEI-SV	155	****	****	****	****	0	****	-30.89	****	_	
ARB-SV	160	****	****	****	****	30.89	****	-30.89		-	-
					271	- 365 Days					
Site-Adjusted Analysis	3										
ACEI-SV	126	****	****	****	****	0	****	0	****		
ARB-SV	183	****	****	****	****	0	****	0		-	_
Fixed Ratio 1:1 Proper	nsity Score Mat	ched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	20	****	****	****	****	0	****	0	****		
ARB-SV	20	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Proper	nsity Score Mat	ched Unco	nditional A	nalysis; Cali	per= 0.05						
ACEI-SV	114	****	****	****	****	0	****	0	****		
ARB-SV	107	****	****	****	****	0	****	U		-	-
Race: Black											
						Overall					
Site-Adjusted Analysis	3										
ACEI-SV	8,897	****	****	****	****	5.61	****	0.76	****	1.15 (0.52, 2.57)	0.727
ARB-SV	6,877	****	****	****	****	4.86	****	0.70		1.13 (0.32, 2.37)	0.727
Fixed Ratio 1:1 Proper	nsity Score Mat	ched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	6,301	****	****	****	****	11.7	****	7.44	****	2.75 / 0.00 0.04\	0.093
ARB-SV	6,301	****	****	****	****	4.25	****	7.44	1. 1. 4. 4. 4. 4.	2.75 (0.88, 8.64)	0.083

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

	Number of	Person Years	Average Person Days	Average Person Years	Number of	Incidence Rate per 1,000 Person	Risk per 1,000	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	•										
ACEI-SV	6,301	****	****	****	****	6.76	****	2	****	1.43 (0.61, 3.35)	0.407
ARB-SV	6,301	****	****	****	****	4.76	****			1.15 (0.01) 0.05)	0.107
					0	- 30 Days					
Site-Adjusted Analys											
ACEI-SV	8,897	****	****	****	****	12.08	****	6.2	****	2.07 (0.55, 7.79)	0.284
ARB-SV	6,877	****	****	****	****	5.88	****	0.2		2.07 (0.33, 7.73)	0.284
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	6,301	****	****	****	****	16.47	****	0.44	****	2 22 / 0 60 0 02)	0.22
ARB-SV	6,301	****	****	****	****	7.06	****	9.41	4. 4. 4. 4. 4.	2.33 (0.60, 9.02)	0.22
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	6,301	****	****	****	****	14.96	****	0.54	****	2.24 (0.60 , 0.05)	0.240
ARB-SV	6,301	****	****	****	****	6.42	****	8.54	40 40 40 40	2.34 (0.60, 9.05)	0.218
	·				31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV	7,131	****	****	****	****	10.81	****	F 24	****	4.04 (0.07, 0.06)	0.430
ARB-SV	5,471	****	****	****	****	5.61	****	5.21	****	1.91 (0.37, 9.86)	0.438
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	4,007	****	****	****	****	13.74	****		ale ale ale ale	/	
ARB-SV	4,007	****	****	****	****	4.58	****	9.16	****	3.00 (0.31, 28.84)	0.341
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	5,035	****	****	****	****	12.15	****	6.03	****	4.00 / 0.27 40.00\	0.426
ARB-SV	5,012	****	****	****	****	6.12	****	6.03	nen nen nen nen	1.99 (0.37, 10.88)	0.426

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

			Average	Average		Incidence Rate per		Incidence Rate Difference	Difference in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
Site-Adjusted Analy											
ACEI-SV	4,319	****	****	****	****	0	****	-8.17	****	_	_
ARB-SV	3,357	****	****	****	****	8.17	****	0.17			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	1,556	****	****	****	****	0	****	0	****		
ARB-SV	1,556	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	3,121	****	****	****	****	0	****	9.03	****		
ARB-SV	3,074	****	****	****	****	8.92	****	-8.92		-	-
					91	- 180 Days					
Site-Adjusted Analy	sis										
ACEI-SV	3,257	****	****	****	****	1.69	****	٥٢	****	0.76 / 0.05 12.20)	0.848
ARB-SV	2,566	****	****	****	****	2.19	****	-0.5		0.76 (0.05, 12.20)	0.040
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	881	****	****	****	****	8.04	****	0.04	****		
ARB-SV	881	****	****	****	****	0	****	8.04	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	2,362	****	****	****	****	2.32	****	0.06	****	0.07/0.06 45 57\	0.005
ARB-SV	2,353	****	****	****	****	2.38	****	-0.06	71. 11. 11. 11.	0.97 (0.06, 15.57)	0.985
					181	- 270 Days					
Site-Adjusted Analy	sis					•					
ACEI-SV	1,845	****	****	****	****	2.7	****	-0.8	****	0.77 / 0.05 13.34\	0.85
ARB-SV	1,418	****	****	****	****	3.5	****	-0.8		0.77 (0.05, 12.24)	0.85

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	299	****	****	****	****	0	****		****		
ARB-SV	299	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	1,348	****	****	****	****	3.68	****	0.42	****	0.00 / 0.05 45 64)	0.006
ARB-SV	1,310	****	****	****	****	3.8	****	-0.12	****	0.98 (0.06, 15.61)	0.986
					271	- 365 Days					
Site-Adjusted Analys	is										
ACEI-SV	1,243	****	****	****	****	0	****	-4.89	****		
ARB-SV	962	****	****	****	****	4.89	****	-4.89		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	133	****	****	****	****	0	****		****		
ARB-SV	133	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	908	****	****	****	****	0	****	0	****		
ARB-SV	886	****	****	****	****	0	****	0		-	-
Race: Pacific Islande	r										
					1	Overall					
Site-Adjusted Analys	is										
ACEI-SV	66	****	****	****	****	52.19	****	52.19	****		
ARB-SV	59	****	****	****	****	0	****	32.19		<u>-</u>	
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ¹						
ACEI-SV	50	****	****	****	****	0	****	0	****		
ARB-SV	50	****	****	****	****	0	****	0	77 77 77 77	-	-

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Unco	onditional A	nalysis; Cal	iper= 0.05					,	
ACEI-SV	50	****	****	****	****	0	****	_	****		
ARB-SV	50	****	****	****	****	0	****	0	****	-	-
					0 -	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV	66	****	****	****	****	0	****	0	****		
ARB-SV	59	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ¹						
ACEI-SV	50	****	****	****	****	0	****	0	****		
ARB-SV	50	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	50	****	****	****	****	0	****	0	****		
ARB-SV	50	****	****	****	****	0	****	U		-	
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV	53	****	****	****	****	0	****	0	****	_	_
ARB-SV	51	****	****	****	****	0	****				_
Fixed Ratio 1:1 Prop	ensity Score Mat	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ¹						
ACEI-SV	37	****	****	****	****	0	****	0	****		
ARB-SV	37	****	****	****	****	0	****	0		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Mat				•						
ACEI-SV	40	****	****	****	****	0	****	0	****	_	_
ARB-SV	44	****	****	****	****	0	****	U		_	_

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Cita Adiusted Analy	·oio				91	- 90 Days					
ACEI-SV ARB-SV	37 34	****	****	****	****	364.96 0	****	364.96	****	-	-
Fixed Ratio 1:1 Prop	pensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ¹						
ACEI-SV	16	****	****	****	****	0	****	0	****		
ARB-SV	16	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	pensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	27	****	****	****	****	0	****	0	****	_	_
ARB-SV	31	****	****	****	****	0	****				
					91	- 180 Days					
Site-Adjusted Analy											
ACEI-SV	31	****	****	****	****	0	****	0	****	_	_
ARB-SV	22	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	pensity Score Ma	tched Con	ditional Ana	lysis; Calipe							
ACEI-SV	11	****	****	****	****	0	****	0	****		
ARB-SV	11	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	pensity Score Ma				•						
ACEI-SV	24	****	****	****	****	0	****	0	****	_	_
ARB-SV	18	****	****	****	****	0	****	U		_	_

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Wieulcai Froduct	ivew Osers	αι Νίοκ	at Nisk	αι ινιον		- 270 Days	New Osers	ieais	ivew osers	iiiteivaij	r-value
Site-Adjusted Analy	sis				101	. 270 Days					
ACEI-SV	16	****	****	****	****	0	****	_			
ARB-SV	13	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Con	ditional Ana	lvsis: Calipe	er= 0.05 ¹						
ACEI-SV	****	****	****	****	****	0	****	_	****		
ARB-SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	12	****	****	****	****	0	****	0	****		
ARB-SV	****	****	****	****	****	0	****	0	4.4.4.4.4.	-	-
					271	- 365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	****	****	****	****	****	0	****	0	****		
ARB-SV	****	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ¹						
ACEI-SV	****	****	****	****	****	0	****	0	****		
ARB-SV	****	****	****	****	****	0	****	0	4.4.4.4.4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	****	****	****	****	****	0	****	0	****		
ARB-SV	****	****	****	****	****	0	****	0		<u>-</u>	
Race: White											
						Overall					
Site-Adjusted Analy	sis										
ACEI-SV	47,666	****	****	****	****	1.79	****	-0.69	****	0.73 (0.44, 1.21)	0.218
ARB-SV	32,431	****	****	****	****	2.48	****	-0.05		0.73 (0.77, 1.21)	0.210

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ¹					•	
ACEI-SV	31,449	****	****	****	****	2.09	****	0.50	****	0.00 / 0.07 . 4.74)	0.555
ARB-SV	31,449	****	****	****	****	2.62	****	-0.52	****	0.80 (0.37, 1.71)	0.565
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	31,449	****	****	****	****	1.6	****	0.07	****	0.65 / 0.36 1.17)	0.151
ARB-SV	31,449	****	****	****	****	2.46	****	-0.87		0.65 (0.36, 1.17)	0.151
					0	- 30 Days					
Site-Adjusted Analys											
ACEI-SV	47,666	****	****	****	****	2.52	****	-1.19	****	0.69 (0.27, 1.73)	0.425
ARB-SV	32,431	****	****	****	****	3.7	****	1.15		0.03 (0.27, 1.73)	0.425
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ¹						
ACEI-SV	31,449	****	****	****	****	3.71	****	0.46	****	1.14 (0.41, 3.15)	0.796
ARB-SV	31,449	****	****	****	****	3.25	****	0.40		1.14 (0.41, 3.13)	0.790
Fixed Ratio 1:1 Prop	ensity Score Mat			nalysis; Cal	•						
ACEI-SV	31,449	****	****	****	****	3.4	****	0.01	****	1.00 (0.38, 2.67)	0.996
ARB-SV	31,449	****	****	****	****	3.39	****	0.01		1.00 (0.38, 2.07)	0.990
					31	- 60 Days					
Site-Adjusted Analys											
ACEI-SV	38,991	****	****	****	****	1.88	****	-1.43	****	0.56 (0.17, 1.83)	0.338
ARB-SV	26,458	****	****	****	****	3.3	****	-1.45		0.50 (0.17, 1.85)	0.556
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ¹						
ACEI-SV	20,913	****	****	****	****	0.82	****	-3.27	****	0.20 (0.02, 1.71)	0.142
ARB-SV	20,913	****	****	****	****	4.08	****	-3.27		0.20 (0.02, 1.71)	0.142
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	25,564	****	****	****	****	0.57	****	-2.83	****	0.17 (0.02, 1.40)	0.099
ARB-SV	25,704	****	****	****	****	3.4	****	-2.03		0.17 (0.02, 1.40)	0.033

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days				,	
Site-Adjusted Analy	sis										
ACEI-SV	26,687	****	****	****	****	2.5	****	-0.42	****	0.05 / 0.32 3.10\	0.815
ARB-SV	18,263	****	****	****	****	2.93	****	-0.42	7777	0.85 (0.23, 3.18)	0.815
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	9,915	****	****	****	****	2.94	****	0	****	1.00 / 0.14 7.10)	1
ARB-SV	9,915	****	****	****	****	2.94	****	0		1.00 (0.14, 7.10)	1
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	17,489	****	****	****	****	2.3	****	-0.71	****	0.76 (0.17, 3.41)	0.723
ARB-SV	17,761	****	****	****	****	3.01	****	-0.71		0.76 (0.17, 3.41)	0.723
					91	- 180 Days					
Site-Adjusted Analy	sis										
ACEI-SV	21,713	****	****	****	****	0.48	****	-2	****	0.20 (0.04, 0.95)	0.043
ARB-SV	14,919	****	****	****	****	2.48	****	-2		0.20 (0.04, 0.93)	0.043
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	6,608	****	****	****	****	1	****	0	****	1 00 / 0 06 15 00\	1
ARB-SV	6,608	****	****	****	****	1	****	U		1.00 (0.06, 15.99)	1
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	14,197	****	****	****	****	0.74	****	-1.81	****	0.29 (0.06, 1.40)	0.123
ARB-SV	14,521	****	****	****	****	2.55	****	-1.01		0.23 (0.00, 1.40)	0.123
					181	- 270 Days					
Site-Adjusted Analy											
ACEI-SV	13,670	****	****	****	****	2.14	****	1.07	****	2.02 (0.41, 10.01)	0.389
ARB-SV	9,226	****	****	****	****	1.07	****	1.07		2.02 (0.71, 10.01)	0.303

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Table 4. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²					-	
ACEI-SV	2,617	*****	*****	****	*****	0	****	0	****	-	-
ARB-SV Fixed Ratio 1:1 Prop	2,617 ensity Score Ma					U					
ACEI-SV	8,929	****	****	****	****	1.65	****	0.55	****	4.54 / 0.35 . 0.04)	0.654
ARB-SV	8,979	****	****	****	****	1.1	****	0.55	4 4 4 4	1.51 (0.25, 9.04)	0.651
					271	- 365 Days					
Site-Adjusted Analys	sis										
ACEI-SV	9,611	****	****	****	****	1.88	****	1 16	****	2.65 (0.20, 22.71)	0.202
ARB-SV	6,362	****	****	****	****	0.72	****	1.16		2.65 (0.30, 23.71)	0.383
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	1,254	****	****	****	****	0	****	0	****		
ARB-SV	1,254	****	****	****	****	0	****	0	41 41 41 41	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	6,159	****	****	****	****	0.74	****	0	****	1.01 / 0.06 16.07)	0.007
ARB-SV	6,198	****	****	****	****	0.74	****	0	ter cer recited ter	1.01 (0.06, 16.07)	0.997

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
						Overall					
Site-Adjusted Analys											
ACEI-SV	68,829	****	****	****	****	2.15	****	0.78	****	1.60 (0.96, 2.66)	0.069
SV	43,140	****	****	****	****	1.36	****	0.76		1.00 (0.30, 2.00)	0.005
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	41,518	****	****	****	****	2.91	****	1.59	****	2.20/1.04 4.65\	0.020
SV	41,518	****	****	****	****	1.32	****	1.59		2.20 (1.04, 4.65)	0.039
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	41,518	****	****	****	****	2.06	****	0.79	****	1.62 (0.91, 2.89)	0.103
SV	41,518	****	****	****	****	1.27	****	0.79		1.02 (0.91, 2.09)	0.105
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV	68,829	****	****	****	****	3.5	****	2.33	****	2.98 (1.01, 8.80)	0.048
SV	43,140	****	****	****	****	1.17	****	2.55		2.36 (1.01, 0.00)	0.040
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	41,518	****	****	****	****	3.68	****	2.24	****	2.75 / 0.00 0.64)	0.002
SV	41,518	****	****	****	****	1.34	****	2.34		2.75 (0.88, 8.64)	0.083
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	41,518	****	****	****	****	3.56	****	2.34	****	2.92 (0.93, 9.18)	0.066
SV	41,518	****	****	****	****	1.21	****	2.54		2.92 (0.95, 9.16)	0.000
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV	55,600	****	****	****	****	3.18	****	1.66	****	2.10 (0.68, 6.50)	0.2
SV	39,259	****	****	****	****	1.52	****	1.00		2.10 (0.00, 0.30)	0.2
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	30,516	****	****	****	****	3.44	****	1.72	****	2.00 / 0.50 0.00)	0.227
SV	30,516	****	****	****	****	1.72	****	1./∠		2.00 (0.50, 8.00)	0.327
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cali							
ACEI-SV	33,361	****	****	****	****	3.1	****	1.53	****	1.96 (0.57, 6.69)	0.284
SV	37,889	****	****	****	****	1.57	****	1.33		1.30 (0.37, 0.03)	0.204

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

•					•						
								Incidence			
			_	_		Incidence		Rate	Difference		
		_	Average	Average		Rate per		Difference	in	Hannad Batta	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
ite-Adjusted Analys											
ACEI-SV	37,527	****	****	****	****	2.5	****	0.43	****	1.21 (0.35, 4.12)	0.766
SV	25,725	****	****	****	****	2.07	****				
ixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV	13,424	****	****	****	****	1.09	****	0	****	1.00 (0.06, 15.99)	1
SV	13,424	****	****	****	****	1.09	****			1.00 (0.00, 13.33)	±
ixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV	22,364	****	****	****	****	1.81	****	-0.33	****	0.84 (0.19, 3.75)	0.82
SV	24,864	****	****	****	****	2.14	****	0.55		0.04 (0.13, 3.73)	0.02
					91	- 180 Days					
Site-Adjusted Analys											
ACEI-SV	30,162	****	****	****	****	0.52	****	-1.11	****	0.33 (0.08, 1.30)	0.113
SV	20,877	****	****	****	****	1.63	****	1.11		0.55 (0.00, 1.50)	0.113
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	8,688	****	****	****	****	1.66	****	0.83	****	2.00 (0.18, 22.06)	0.571
SV	8,688	****	****	****	****	0.83	****	0.65		2.00 (0.18, 22.00)	0.371
ixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	17,798	****	****	****	****	0.6	****	-0.52	****	0.53 (0.10, 2.90)	0.465
SV	20,213	****	****	****	****	1.12	****	-0.32		0.33 (0.10, 2.30)	0.403
					181	- 270 Days					
Site-Adjusted Analys	sis										
ACEI-SV	18,794	****	****	****	****	1.82	****	0.91	****	1.97 (0.41, 9.47)	0.399
SV	11,373	****	****	****	****	0.91	****	0.91		1.97 (0.41, 9.47)	0.333
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	2,885	****	****	****	****	0	****	2.12	****		
		****	****	****	****	2.12	****	-2.12	181 181 181 181 181	-	-
SV	2,885	****				2.12					
					iper= 0.05	2.12					
SV Fixed Ratio 1:1 Prop ACEI-SV					iper= 0.05 ****	1.39	****	0.46	****	1.46 (0.24, 8.72)	0.681

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

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					271	- 365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	13,146	****	****	****	****	1.72	****	1.06	****	2.57 (0.30, 21.97)	0.39
SV	7,133	****	****	****	****	0.66	****	1.00		2.57 (0.50, 21.97)	0.59
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	1,270	****	****	****	****	8.45	****	0.45	****		
SV	1,270	****	****	****	****	0	****	8.45		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	7,231	****	****	****	****	1.91	****	1 24	****	2.76 / 0.20 26 50\	0.29
SV	6,972	****	****	****	****	0.67	****	1.24		2.76 (0.29, 26.50)	0.38

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

						Insidence		Incidence	D:#forese		
			Average	Average		Incidence Rate per		Rate Difference	Difference in		
		Person	Average Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
No Angioedema (-1		at NISK	at NISK	at NISK	Events	Tears	New Osers	Tears	New Osers	intervarj	r-value
Tto Anglocacina (1	00, 1,					Overall					
Site-Adjusted Analy	sis										
ACEI-SV	68,746	****	****	****	****	2.07	****	0.00	****	1.00 / 1.00 . 2.20)	0.022
SV	43,081	****	****	****	****	1.11	****	0.96		1.90 (1.09, 3.29)	0.023
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	41,454	****	****	****	****	2.91	****	1.00	****	2 14 / 1 24 7 26)	0.008
SV	41,454	****	****	****	****	0.93	****	1.99		3.14 (1.34, 7.36)	0.008
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	41,454	****	****	****	****	2.06	****	1.06	****	2.05 (1.10, 3.82)	0.024
SV	41,454	****	****	****	****	1.01	****	1.00		2.03 (1.10, 3.82)	0.024
					0	- 30 Days					
Site-Adjusted Analy	sis										
ACEI-SV	68,746	****	****	****	****	3.31	****	2.73	****	5.61 (1.30, 24.29)	0.021
SV	43,081	****	****	****	****	0.59	****	2.75		3.01 (2.30) 2 1.23)	0.021
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV	41,454	****	****	****	****	3.68	****	3.01	****	5.50 (1.22, 24.81)	0.027
SV	41,454	****	****	****	****	0.67	****	5.01		5.50 (1.22, 24.01)	0.027
Fixed Ratio 1:1 Prop	ensity Score Ma				-						
ACEI-SV	41,454	****	****	****	****	3.56	****	2.96	****	5.83 (1.29, 26.32)	0.022
SV	41,454	****	****	****	****	0.61	****	2.50		3.03 (1.23, 20.32)	0.022
a					31	- 60 Days					
Site-Adjusted Analy											
ACEI-SV	55,530	****	****	****	****	2.92	****	1.4	****	1.92 (0.61, 6.03)	0.264
SV	39,207	****	****	****	****	1.52	****	=		(2:2-, 2:33)	

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Table 6. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	30,472	****	****	****	****	3.45	****	1.72	****	2.00 (0.50, 8.00)	0.327
SV	30,472	****	****	****	****	1.72	****	1.72		2.00 (0.50, 8.00)	0.327
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV	33,309	****	****	****	****	3.1	****	1.53	****	1.96 (0.57, 6.69)	0.284
SV	37,832	****	****	****	****	1.57	****	1.55		1.90 (0.57, 0.09)	0.264
					61	- 90 Days					
Site-Adjusted Analys	is										
ACEI-SV	37,484	****	****	****	****	2.51	****	0.95	****	1.61 (0.42, 6.22)	0.491
SV	25,688	****	****	****	****	1.56	****	0.55		1.01 (0.42, 0.22)	0.431
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	13,401	****	****	****	****	1.1	****	0	****	1.00 (0.06, 15.99)	1
SV	13,401	****	****	****	****	1.1	****	U		1.00 (0.06, 15.99)	1
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV	22,332	****	****	****	****	1.81	****	0.2	****	1.12 (0.23, 5.55)	0.89
SV	24,823	****	****	****	****	1.61	****	0.2		1.12 (0.23, 3.33)	0.89
					91 -	- 180 Days					
Site-Adjusted Analys											
ACEI-SV	30,132	****	****	****	****	0.52	****	-0.84	****	0.39 (0.09, 1.65)	0.201
SV	20,847	****	****	****	****	1.36	****	0.04		0.55 (0.05, 1.05)	0.201
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	8,674	****	****	****	****	1.66	****	1 66	****		
SV	8,674	****	****	****	****	0	****	1.66		<u>-</u>	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV	17,773	****	****	****	****	0.6	****	-0.24	****	0.71 (0.12, 4.25)	0.708
SV	20,180	****	****	****	****	0.84	****	-0.24		0.71 (0.12, 4.23)	0.700

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Table 6. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

-								Incidence			
				A		Incidence		Rate	Difference		
		_	Average	Average		Rate per	5.1	Difference	in	Hazard Ratio	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	(95% Confidence	Wald
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	-	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
	•				181	- 270 Days					
Site-Adjusted Analy		****	****	****	****	4.00	****				
ACEI-SV	18,772	****	****	****	****	1.82	****	0.91	****	1.97 (0.41, 9.46)	0.399
SV	11,356					0.91	****				
Fixed Ratio 1:1 Prop											
ACEI-SV	2,887	****	****	****	****	0	****	-2.11	****	_	_
SV	2,887	****	****	****	****	2.11	****	2.11			
Fixed Ratio 1:1 Prop					•						
ACEI-SV	10,707	****	****	****	****	1.39	****	0.46	****	1.46 (0.24, 8.72)	0.681
SV	11,052	****	****	****	****	0.93	****	0.40		1.40 (0.24, 0.72)	0.001
					271	- 365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	13,129	****	****	****	****	1.72	****	1.06	****	2.56 (0.30, 21.95)	0.39
SV	7,122	****	****	****	****	0.66	****	1.00		2.30 (0.30, 21.93)	0.39
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	1,269	****	****	****	****	8.46	****	0.46	****		
SV	1,269	****	****	****	****	0	****	8.46	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	7,219	****	****	****	****	1.91	****	1.24	****	2.75 / 0.20, 26, 40\	0.20
SV	6,959	****	****	****	****	0.67	****	1.24	4.4.4.4.4.	2.75 (0.29, 26.48)	0.38
Angioedema (-183, -											
						Overall					
Site-Adjusted Analy	sis										
ACEI-SV	83	****	****	****	****	72.23	****	405.24	****	0.40/0.07. 3.47\	0.207
SV	59	****	****	****	****	177.54	****	-105.31	4, 4, 4, 4, 4,	0.40 (0.07, 2.17)	0.287

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Table 6. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

Medical Product Fixed Ratio 1:1 Prop	38	Person Years at Risk tched Cond *****	Average Person Days at Risk ditional Ana *****	Average Person Years at Risk lysis; Calipe *****	Number of Events er= 0.05 ² *****	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) ¹	Wald P-Value ¹ -
SV	38					133.51	****				
Fixed Ratio 1:1 Prop ACEI-SV SV	38 38	***** ****	***** *****	***** *****	***** ****	0 131.41	****	-131.41	****	-	-
					0	- 30 Days					
Site-Adjusted Analy	sis										
ACEI-SV SV	83 59	****	****	****	****	155.04 429.18	****	-274.15	****	0.36 (0.03, 3.98)	0.405
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Calipe	er= 0.05 ²						
ACEI-SV SV	38 38	****	*****	****	****	0	****	0	****	-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV SV	38 38	*****	****	*****	*****	0 0	****	0	****	-	-
					31	- 60 Days					
Site-Adjusted Analy	sis										
ACEI-SV SV	74 54	*****	****	****	*****	186.22 0	****	186.22	****	-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Caline	er= 0.05 ²						
ACEI-SV	32	****	****	****	****	0	****		****		
SV	32	****	****	****	****	0	****	0	****	-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	34	****	****	****	****	0	****	0	****		
SV	36	****	****	****	****	0	****	U		-	-

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Table 6. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

(100) 1, 11111								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
	11011 03013	ut mon	ut mon	ut mon		- 90 Days	11011 05015		THE WOOLE		· value
Site-Adjusted Analy	sis										
ACEI-SV	47	****	****	****	****	0	****	242.42	****		
SV	39	****	****	****	****	348.43	****	-348.43	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	27	****	****	****	****	0	****	757.50	****		
SV	27	****	****	****	****	757.58	****	-757.58	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	23	****	****	****	****	0	****	490.77	****		
SV	29	****	****	****	****	480.77	****	-480.77		-	-
					91	- 180 Days					
Site-Adjusted Analy	sis										
ACEI-SV	34	****	****	****	****	0	****	-159.24	****	_	_
SV	31	****	****	****	****	159.24	****	-133.24			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	12	****	****	****	****	0	****	0	****	_	_
SV	12	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV	19	****	****	****	****	0	****	-228.31	****	_	_
SV	22	****	****	****	****	228.31	****	220.51			
					181	- 270 Days					
Site-Adjusted Analy											
ACEI-SV	23	****	****	****	****	0	****	0	****	-	_
SV	20	****	****	****	****	0	****	•			

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Table 6. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	12	****	****	****	****	0	****	0	****		
SV	16	****	****	****	****	0	****	0		-	-
					271	- 365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	19	****	****	****	****	0	****	0	****		
SV	14	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	11	****	****	****	****	0	****	0	****		
SV	11	****	****	****	****	0	****	0	ter cer recited ter	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

	Number of	Person Years	Average Person Days	Average Person Years	Number of	Incidence Rate per 1,000 Person	Risk per 1,000	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Unknown											
						Overall					
Site-Adjusted Analy											
ACEI-SV	11,333	****	****	****	****	1.28	****	0.52	****	1.75 (0.34, 9.03)	0.504
SV	7,114	****	****	****	****	0.76	****				
Fixed Ratio 1:1 Prop	pensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	6,597	****	****	****	****	1.67	****	0.84	****	2.00 (0.18, 22.06)	0.571
SV	6,597	****	****	****	****	0.84	****	0.64		2.00 (0.18, 22.00)	0.571
Fixed Ratio 1:1 Prop	pensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	6,597	****	****	****	****	1.37	****	0.97	****	3.43 (0.36, 33.01)	0.286
SV	6,597	****	****	****	****	0.41	****	0.97		3.43 (0.30, 33.01)	0.280
					0	- 30 Days					
Site-Adjusted Analy	/sis										
ACEI-SV	11,333	****	****	****	****	1.21	****	1.21	****		
SV	7,114	****	****	****	****	0	****	1.21		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	6,597	****	****	****	****	0	****		****		
SV	6,597	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	6,597	****	****	****	****	0	****	0	****		
SV	6,597	****	****	****	****	0	****	0	ጥ ጥ ጥ ጥ	-	-
	•				31	- 60 Days					
Site-Adjusted Analy	/sis										
ACEI-SV	8,756	****	****	****	****	3.33	****				
SV	6,412	****	****	****	****	0	****	3.33	****	-	-

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

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop						Tears	New Osers	Tears	New Osers	ilitervalj	r-value
ACEI-SV	4,632	****	*****	****	****	3.69	****				
SV	4,632	****	****	****	****	0	****	3.69	****	-	-
Fixed Ratio 1:1 Prop	•	tched Unc	onditional A	nalysis: Cali	iner= 0 05						
ACEI-SV	5.084	****	****	****	****	5.75	****				
SV	5,989	****	****	****	****	0	****	5.75	****	-	-
3.	3,363				61	- 90 Days					
Site-Adjusted Analy	sis					30 24,5					
ACEI-SV	6,037	****	****	****	****	2.23	****				
SV	4,335	****	****	****	****	3.08	****	-0.85	****	0.71 (0.04, 11.29)	0.805
Fixed Ratio 1:1 Prop		tched Cond	ditional Ana	lysis: Caline	r= 0.05 ²						
ACEI-SV	2,148	****	****	****	****	6.89	****				
SV	2,148	****	****	****	****	6.89	****	0	****	1.00 (0.06, 15.99)	1
Fixed Ratio 1:1 Prop	•	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	3,481	****	****	****	****	3.9	****	0.64	****	1 10 (0 07 10 05)	2.222
SV	4,056	****	****	****	****	3.29	****	0.61	****	1.19 (0.07, 19.05)	0.902
	·				91	- 180 Days					
Site-Adjusted Analy	sis					_					
ACEI-SV	4,815	****	****	****	****	0	****	1.50	****		
SV	3,512	****	****	****	****	1.56	****	-1.56		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	1,367	****	****	****	****	0	****		****		
SV	1,367	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	2,731	****	****	****	****	0	****				
SV	3,285	****	****	****	****	0	****	0	****	-	-



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

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) ¹	Wald P-Value ¹
						- 270 Days					
Site-Adjusted Analy	rsis										
ACEI-SV	3,039	****	****	****	****	0	****		****		
SV	2,015	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	488	****	****	****	****	0	****		****		
SV	488	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	1,668	****	****	****	****	0	****	0	****		
SV	1,901	****	****	****	****	0	****	0		-	-
					271	- 365 Days					
Site-Adjusted Analy	rsis										
ACEI-SV	2,127	****	****	****	****	2.13	****	2.13	****		
SV	1,276	****	****	****	****	0	****	2.13		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	217	****	****	****	****	0	****	0	****		
SV	217	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	1,130	244.26	78.95	0.22	0	0	****	0	****		
SV	1,212	260.05	78.37	0.21	0	0	****			-	
Race: American Ind	ian										
						Overall					
Site-Adjusted Analy	rsis										
ACEI-SV	237	****	****	****	****	0	****	0	****	_	_
SV	139	****	****	****	****	0	****	U		-	-

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

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	117	****	****	****	****	0	****	0	****		
SV	117	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	117	****	****	****	****	0	****	0	****		
SV	117	****	****	****	****	0	****	0		-	
					0	- 30 Days					
Site-Adjusted Analy											
ACEI-SV	237	****	****	****	****	0	****	0	****	_	_
SV	139	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	117	****	****	****	****	0	****	0	****		
SV	117	****	****	****	****	0	****	0		_	_
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV	117	****	****	****	****	0	****	0	****	_	_
SV	117	****	****	****	****	0	****				
					31	- 60 Days					
Site-Adjusted Analy											
ACEI-SV	188	****	****	****	****	0	****	0	****	_	_
SV	121	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV	84	****	****	****	****	0	****	0	****		
SV	84	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma		onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	97	****	****	****	****	0	****	0	****		
SV	101	****	****	****	****	0	****	U		-	-

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

								Incidence			
			A.,	Aveners		Incidence		Rate Difference	Difference		
		Davasa	Average	Average	Maraka	Rate per	Dieloman		in Bisk nor	Hazard Ratio	
	N	Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	(95% Confidence	Wald
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	•	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
	•				61	90 Days					
Site-Adjusted Analy		****	****	****	****		****				
ACEI-SV	121					0		0	****	-	-
SV	83	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop											
ACEI-SV	34	****	****	****	****	0	****	0	****	_	_
SV	34	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop											
ACEI-SV	57	****	****	****	****	0	****	0	****	_	_
SV	66	****	****	****	****	0	****	0			
					91	- 180 Days					
Site-Adjusted Analy											
ACEI-SV	98	****	****	****	****	0	****	0	****		_
SV	62	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	21	****	****	****	****	0	****	0	****		
SV	21	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	45	****	****	****	****	0	****		****		
SV	53	****	****	****	****	0	****	0	****	-	-
					181	270 Days					
Site-Adjusted Analy	sis					•					
ACEI-SV	55	****	****	****	****	0	****	_	****		
SV	33	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis: Caline	r= 0.05 ²	-					
ACEI-SV	****	****	****	****	****	0	****				
SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis: Cali	iner= 0.05	<u> </u>					
ACEI-SV	22	****	****	****	****	0	****				
		****	****	****	****	·	****	0	****	-	-
SV	30	ጥጥጥጥ	***	ጥጥጥጥ	ጥጥጥጥ	0	ጥጥጥጥ				

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

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) ¹	Wald P-Value ¹
					271	- 365 Days					
Site-Adjusted Analys	is										
ACEI-SV	39	****	****	****	****	0	****	0	****		
SV	18	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	15	****	****	****	****	0	****	0	****	_	_
SV	16	****	****	****	****	0	****	<u> </u>			
Race: Asian											
						Overall					
Site-Adjusted Analys		****	****	****	****		****				
ACEI-SV	664	****	****	****	****	0	****	0	****	-	-
SV	531					0	****				
Fixed Ratio 1:1 Prope		tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	459	****	****	****	****	0	****	0	****	-	_
SV	459	****	****	****	****	0	****				
Fixed Ratio 1:1 Prope	-										
ACEI-SV	459	****	****	****	****	0	****	0	****		
	459	****	****	****	****		****	0	71 71 71 71	-	-

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

	Number of	Person Years	Average Person Days	Average Person Years	Number of	Incidence Rate per 1,000 Person	Risk per 1,000	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Cite Adirected Accele	- • -				0	- 30 Days					
Site-Adjusted Analys ACEI-SV	664	****	****	****	****	0	****				
	531	****	****	****	****	0	****	0	****	-	-
SV						U					
Fixed Ratio 1:1 Prop		tched Cond	litional Ana *****	lysis; Calipe	r= 0.05 ⁻		****				
ACEI-SV	459	****	****	****	*****	0	****	0	****	-	-
SV	459					0	****				
Fixed Ratio 1:1 Prop		****	****	naiysis; Caii	*****		****				
ACEI-SV	459	****	****	****	****	0	****	0	****	-	-
SV	459	****	****	****		0 - 60 Days	*****				
Site-Adjusted Analys	oic .				51	- 60 Days					
ACEI-SV	511	****	****	****	****	0	****				
SV	490	****	****	****	****	0	****	0	****	-	-
		4-bd-C	lisianal Ana	husia. Calina	0.0F ²						
Fixed Ratio 1:1 Prop	325	****	****	*****	*****	0	****				
ACEI-SV		****	****	****	****	•	****	0	****	-	-
SV Fixed Ratio 1:1 Prop	325					0					
ACEI-SV	354	*****	*****	*****	*****	0	****				
SV	422	****	****	****	****	0	****	0	****	-	-
31	422					- 90 Days					
Site-Adjusted Analys	sis				01	- JU Days					
ACEI-SV	352	****	****	****	****	0	****				
SV	333	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Cond	litional Ana	lveie: Calina	r= 0.05 ²						
ACEI-SV	150	****	*****	****	****	0	****				
SV	150	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop						U					
ACEI-SV	247	****	****	*****	*****	0	****				
SV	285	****	****	****	****	0	****	0	****	-	-

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

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) ¹	Wald P-Value ¹
ivieuicai Product	New Osers	at NISK	at NISK	at KISK		- 180 Days	New Osers	Tears	New Osers	intervaij	P-value
Site-Adjusted Analy	sis				71	- 100 Days					
ACEI-SV	268	****	****	****	****	0	****				
SV	254	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Cond	litional Ana	lysis: Caline	r= 0.05 ²						
ACEI-SV	93	****	****	****	****	0	****				
SV	93	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	195	****	****	****	****	0	****		****		
SV	222	****	****	****	****	0	****	0	****	-	-
					181	- 270 Days					
Site-Adjusted Analy	sis										
ACEI-SV	178	****	****	****	****	0	****	0	****		
SV	138	****	****	****	****	0	****	U		-	_
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	35	****	****	****	****	0	****	0	****		
SV	35	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	126	****	****	****	****	0	****	0	****	_	_
SV	123	****	****	****	****	0	****				
					271	- 365 Days					
Site-Adjusted Analy											
ACEI-SV	127	****	****	****	****	0	****	0	****	-	_
SV	89	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop											
ACEI-SV	17	****	****	****	****	0	****	0	****	<u>-</u>	_
SV	17	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	<u> </u>										
ACEI-SV	88	****	****	****	****	0	****	0	****	-	_
SV	79	****	****	****	****	0	****	Ū			



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

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) ¹	Wald P-Value ¹
Race: Black											
						Overall					
Site-Adjusted Analy											
ACEI-SV	8,906	****	****	****	****	5.61	****	1.55	****	1.43 (0.58, 3.51)	0.434
SV	5,806	****	****	****	****	4.06	****				
Fixed Ratio 1:1 Prop	ensity Score Ma		ditional Ana	lysis; Calipe							
ACEI-SV	5,469	****	****	****	****	5.99	****	1.2	****	1.25 (0.34, 4.65)	0.739
SV	5,469	****	****	****	****	4.79	****	1.2		1.23 (0.34, 4.03)	0.739
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV	5,469	****	****	****	****	3.77	****	0.11	****	1.06 (0.34, 3.29)	0.919
SV	5,469	****	****	****	****	3.66	****	0.11		1.00 (0.34, 3.29)	0.919
					0	- 30 Days					
Site-Adjusted Analy											
ACEI-SV	8,906	****	****	****	****	12.07	****	9.9	****	5.44 (0.68, 43.51)	0.11
SV	5,806	****	****	****	****	2.17	****	5.5		3.44 (0.00, 43.31)	0.11
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	5,469	****	****	****	****	10.15	****	7.61	****	4.00 / 0.45 35 70\	0.215
SV	5,469	****	****	****	****	2.54	****	7.01		4.00 (0.45, 35.79)	0.215
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	5,469	****	****	****	****	9.81	****	7.51	****	4 22 / 0 47 27 99\	0.197
SV	5,469	****	****	****	****	2.31	****	7.51		4.23 (0.47, 37.88)	0.197
					31	60 Days					
Site-Adjusted Analy	sis										
ACEI-SV	7,138	****	****	****	****	10.8	****	7.82	****	3.71 (0.43, 31.76)	0.231
SV	5,277	****	****	****	****	2.98	****	7.02		J./1 (U.43, J1./0)	0.231
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	4,000	****	****	****	****	4.75	****	4.75	****		
SV	4,000	****	****	****	****	0	****	4.75		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	4,389	****	****	****	****	7.06	****	3.91	****	2.35 (0.21, 25.95)	0.485
SV	4,983	****	****	****	****	3.15	****	3.31		2.33 (0.21, 23.93)	0.465

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

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) ¹	Wald P-Value ¹
					61	90 Days					
Site-Adjusted Analy											
ACEI-SV	4,325	****	****	****	****	0	****	-4.49	****	_	_
SV	3,036	****	****	****	****	4.49	****	-4.45			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	1,369	****	****	****	****	0	****	11 12	****		
SV	1,369	****	****	****	****	11.12	****	-11.12		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	2,635	****	****	****	****	0	****	-4.74	****		
SV	2,874	****	****	****	****	4.74	****	-4.74			
					91	- 180 Days					
Site-Adjusted Analy	sis										
ACEI-SV	3,259	****	****	****	****	1.69	****	-3.72	****	0.30 (0.03, 3.36)	0.332
SV	2,303	****	****	****	****	5.41	****	-5.72		0.30 (0.03, 3.30)	0.332
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	789	****	****	****	****	0	****	-10.52	****		
SV	789	****	****	****	****	10.52	****	-10.52		-	-
Fixed Ratio 1:1 Prop	•			nalysis; Cal	•						
ACEI-SV	1,962	****	****	****	****	0	****	-2.83	****	_	
SV	2,190	****	****	****	****	2.83	****	-2.03			
					181	- 270 Days					
Site-Adjusted Analy											
ACEI-SV	1,846	****	****	****	****	2.69	****	-7.3	****	0.27 (0.02, 3.00)	0.287
SV	1,053	****	****	****	****	10	****	,.5		3.27 (3.32, 3.33)	0.207
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV	201	****	****	****	****	0	****	-30.81	****	_	
SV	201	****	****	****	****	30.81	****	-30.61			
Fixed Ratio 1:1 Prop					•						
ACEI-SV	1,072	****	****	****	****	0	****	-10.37	****		
SV	1,015	****	****	****	****	10.37	****	-10.57		-	-

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

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					271	365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	1,245	****	****	****	****	0	****	0	****		
SV	653	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	83	****	****	****	****	0	****	0	****		
SV	83	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	698	****	****	****	****	0	****	0	****		
SV	629	****	****	****	****	0	****	0		-	-

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

								Incidence			
			A	A		Incidence		Rate	Difference		
		_	Average	Average		Rate per	51.1	Difference	in	Hazard Ratio	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per		Wald
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Pacific Islande	er										
						Overall					
Site-Adjusted Analy		****	district district	****	****		****				
ACEI-SV	66		****			52.19		52.19	****	-	_
SV	46	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV	32	****	****	****	****	0	****	0	****	_	_
SV	32	****	****	****	****	0	****	0			_
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cal	•						
ACEI-SV	32	****	****	****	****	0	****	0	****	_	_
SV	32	****	****	****	****	0	****	0			
					0	- 30 Days					
Site-Adjusted Analy	sis										
ACEI-SV	66	****	****	****	****	0	****	0	****	_	_
SV	46	****	****	****	****	0	****	0		_	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	32	****	****	****	****	0	****	0	****		
SV	32	****	****	****	****	0	****	0	4.4.4.4.4	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	32	****	****	****	****	0	****	0	****		
SV	32	****	****	****	****	0	****	0	4, 4, 4, 4, 4,	-	-
					31	- 60 Days					
Site-Adjusted Analy	sis										
ACEI-SV	53	****	****	****	****	0	****	0	****		
SV	42	****	****	****	****	0	****	0	71 71 71 71	-	-

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

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	24	****	****	****	****	0	****	0	****		
SV	24	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	25	****	****	****	****	0	****	0	****		
SV	30	****	****	****	****	0	****	U		-	-
					61	- 90 Days					
Site-Adjusted Analy											
ACEI-SV	36	****	****	****	****	370.37	****	370.37	****	_	_
SV	28	****	****	****	****	0	****	370.37			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	11	****	****	****	****	0	****	0	****		
SV	11	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	15	****	****	****	****	0	****	0	****	_	_
SV	19	****	****	****	****	0	****	0		_	_
					91	- 180 Days					
Site-Adjusted Analys											
ACEI-SV	31	****	****	****	****	0	****	0	****	_	_
SV	24	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	<u> </u>		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV	12	****	****	****	****	0	****	0	****		
SV	17	****	****	****	****	0	****	U		-	-



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

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) ¹	Wald P-Value ¹
					181	- 270 Days				·	
Site-Adjusted Analy	sis										
ACEI-SV	16	****	****	****	****	0	****	0	****		
SV	15	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	***	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	4.4.4.4.4.	-	-
					271	- 365 Days					
Site-Adjusted Analy	sis										
ACEI-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	nan nan nan nan	-	-
Race: White											
						Overall					
Site-Adjusted Analy	sis										
ACEI-SV	47,623	****	****	****	****	1.79	****	0.68	****	1.62 (0.83, 3.16)	0.155
SV	29,504	****	****	****	****	1.11	****	0.00		1.02 (0.03, 3.10)	0.133



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

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	28,510	****	****	****	****	2.78	****	1.05	****	2.00 / 1.00 .0.25\	0.022
SV	28,510	****	****	****	****	0.93	****	1.85		3.00 (1.09, 8.25)	0.033
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV	28,510	****	****	****	****	2	****	0.86	****	174/005 256\	0.129
SV	28,510	****	****	****	****	1.15	****	0.86		1.74 (0.85, 3.56)	0.129
					0 -	· 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV	47,623	****	****	****	****	2.52	****	1.24	****	1.98 (0.54, 7.32)	0.305
SV	29,504	****	****	****	****	1.28	****	1.24		1.36 (0.34, 7.32)	0.303
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV	28,510	****	****	****	****	3.39	****	1.93	****	2 22 / 0 60 0 02)	0.22
SV	28,510	****	****	****	****	1.45	****	1.93		2.33 (0.60, 9.02)	0.22
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV	28,510	****	****	****	****	3.28	****		****	(
								1 ()(2		3 10 1 N E 1 N E 01	Λ 10Λ
SV	28,510	****	****	****	****	1.32	****	1.96	****	2.48 (0.64, 9.58)	0.189
SV	28,510	****	****	****		1.32 - 60 Days	****	1.96	****	2.48 (0.64, 9.58)	0.189
Site-Adjusted Analys	·	****			31			1.96	****	2.48 (0.64, 9.58)	0.189
	·	****	****	****			****		****		
Site-Adjusted Analys ACEI-SV SV	38,957 26,919	****	****	****	**** ****	- 60 Days		0.23		1.13 (0.27, 4.75)	0.189
Site-Adjusted Analys ACEI-SV SV	38,957 26,919	****	****	****	**** ****	- 60 Days	****				
Site-Adjusted Analys	38,957 26,919	****	****	****	**** ****	- 60 Days	****	0.23	****	1.13 (0.27, 4.75)	0.863
Site-Adjusted Analys ACEI-SV SV Fixed Ratio 1:1 Prope	38,957 26,919 ensity Score Ma	**** **** tched Cond	***** *****	***** *****	***** ***** r= 0.05 ²	- 60 Days 1.88 1.65	****				
Site-Adjusted Analys ACEI-SV SV Fixed Ratio 1:1 Property	38,957 26,919 ensity Score Ma 21,212 21,212	***** ***** tched Cond *****	***** ***** ditional Ana *****	***** ***** lysis; Calipe *****	***** ***** r= 0.05 ² *****	1.88 1.65	****	0.23	****	1.13 (0.27, 4.75)	0.863
Site-Adjusted Analys ACEI-SV SV Fixed Ratio 1:1 Property ACEI-SV SV	38,957 26,919 ensity Score Ma 21,212 21,212	***** ***** tched Cond *****	***** ***** ditional Ana *****	***** ***** lysis; Calipe *****	***** ***** r= 0.05 ² *****	1.88 1.65	****	0.23	****	1.13 (0.27, 4.75)	0.863



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

Tullion 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1							Incidence		Incidence Rate	Difference		
Number of Years Days Years Of Person 1,000				Average	Average		Rate per		Difference	in		
Medical Product New Users at Risk at R			Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per		
Site-Adjusted Analysis		Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Site-Adjusted Analysis	Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
ACEI-SV 26,664 ***** ***** ***** 2.51 ***** 1.02 ***** 1.69 (0.33, 8.72) 0.53						61	90 Days					
Section Sect	Site-Adjusted Analy	sis										
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² KERVER Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05² KERVER Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05² KERVER Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05² KACEI-SV 15,760 **** **** **** **** 1.7 ***** 0.18 ***** 1.11 (0.16, 7.88) 0.917 STITE-Adjusted Analysis ACEI-SV 21,696 **** **** **** **** 0.48 ***** 0.67 ***** 0.42 (0.07, 2.53) 0.347 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 6,407 **** **** **** 0.48 ***** 0.67 ***** 0.42 (0.07, 2.53) 0.347 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 12,722 **** **** ***** 0.84 ***** 0.34 ***** 0.71 (0.12, 4.24) 0.706 STITE-Adjusted Analysis Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 12,722 **** **** ***** 0.84 ***** 0.34 ***** 0.71 (0.12, 4.24) 0.706 STITE-Adjusted Analysis Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 2,209 **** **** ***** 0.0 ***** 0.34 ***** 0.71 (0.12, 4.24) 0.706 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 2,209 **** **** ***** 0.0 ***** 0.34 ***** 0.71 (0.12, 4.24) 0.706 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 2,209 **** **** ***** 0.0 ***** 0.34 ***** 0.71 (0.12, 4.24) 0.706 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 2,209 **** **** **** 0.0 ***** 0.34 ***** 0	ACEI-SV	26,664	****	****	****	****	2.51	****	1.02	****	1 60 (0 22 9 72)	0.52
ACEI-SV 9,627 ***** ***** ***** ***** 1.51 ****** 1.51 ****** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51	SV	17,919	****	****	****	****	1.48	****	1.02		1.09 (0.33, 8.72)	0.55
ACEI-SV 9,627 ***** ***** ***** ***** 1.51 ****** 1.51 ****** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51 ***** 1.51	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 15,760 ***** ***** ***** ***** 1.7 ***** 0.18 ***** 1.11 (0.16, 7.88) 0.917 SV 17,368 **** **** **** ***** 1.53 ***** 0.18 ***** 1.11 (0.16, 7.88) 0.917 SITE-Adjusted Analysis ACEI-SV 21,696 ***** **** **** ***** 0.48 ***** 0.67 ***** 0.42 (0.07, 2.53) 0.347 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 6,407 **** **** **** **** 0.84 ***** 0.84* ACEI-SV 6,407 **** **** **** **** 0.84 ***** 0.84* ACEI-SV 12,722 **** **** **** **** 0.84 ***** 0.84* ACEI-SV 12,722 **** **** **** 1.15 ***** 0.84* ACEI-SV 12,722 **** **** **** 1.18 **** 0.84* ACEI-SV 12,722 **** **** **** 1.18 **** 0.84* ACEI-SV 13,667 **** **** **** 1.18 **** 0.84* ACEI-SV 22,09 **** **** **** 0.84* ACEI-SV 2,209 **** **** **** 0.84* ACEI-SV 2,209 **** **** 0.84* ACEI-SV 3,751 **** **** 0.84* ACEI-SV 7,751 **** 0.84* ACEI-							1.51	****	1 [1	****		
ACEI-SV 15,760 ***** **** **** ***** 1.7 ***** 0.18 ***** 1.11 (0.16, 7.88) 0.917 Site-Adjusted Analysis ACEI-SV 21,696 ***** **** **** **** 1.15 ***** 0.67 ***** 0.42 (0.07, 2.53) 0.347 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 12,722 ***** **** ***** ***** 0.84 ***** ACEI-SV 14,288 **** **** ***** 1.18 **** 0.34 ***** 0.71 (0.12, 4.24) 0.706 Site-Adjusted Analysis ACEI-SV 13,667 **** **** ***** 0.84 ***** ACEI-SV 13,667 **** ACEI-SV 13,667 **** ACEI-SV 14,288 **** **** ACEI-SV 13,667 ***** ACEI-SV 13,667 ***** ACEI-SV 13,667 **** ACE	SV	9,627	****	****	****	****	0	****	1.51	4. 4. 4. 4. 4.	-	-
SV	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
SV 17,368 **** **** **** **** 1.53 **** 0.18 1.11 (0.10, 7.89) 0.347 Site-Adjusted Analysis ACEI-SV 21,696 **** **** **** **** 0.48 ****	ACEI-SV	15,760	****	****	****	****	1.7	****	0.10	****	1 11 / 0 16 7 99\	0.017
ACEI-SV 21,696 ***** ***** ***** ***** ***** 1.15 ******	SV	17,368	****	****	****	****	1.53	****	0.18		1.11 (0.16, 7.88)	0.917
ACEI-SV 14,724 ***** ***** ***** ***** 1.15 ***** -0.67 ***** 0.42 (0.07, 2.53) 0.347 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 6,407 **** **** ***** ***** 0 ***** 0 ***** 2.22 *****						91	- 180 Days					
ACEI-SV 14,724 ******	Site-Adjusted Analy	sis										
SV 14,724 ***** **** **** ***** 1.15 ***** **** *	ACEI-SV	21,696	****	****	****	****	0.48	****	0.67	****	0.42 (0.07 - 2.52)	0.247
ACEI-SV 6,407 ***** **** **** **** **** 0 ***** 2.22 ***** 5.00 ***** 2.22 *****	SV	14,724	****	****	****	****	1.15	****	-0.67		0.42 (0.07, 2.55)	0.547
ACEI-SV 6,407 ***** **** **** **** **** 0 ***** 2.22 ***** 5.00 ***** 2.22 *****	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
SV 6,407 ***** **** ***** ***** 0 ***** 2.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 12,722 ***** **** ***** 0.84 ***** -0.34 ***** 0.71 (0.12, 4.24) 0.706 Site-Adjusted Analysis ACEI-SV 13,667 **** **** **** ***** 2.14 ***** 2.14 ***** 5.0 ****** 5.0 ****** 5.0 ******* 5.0 ****** 5.0 ****** 5.0 ****** 5.0 ****							2.22	****	2.22	****		
ACEI-SV 12,722 ***** **** **** **** **** **** ***	SV	6,407	****	****	****	****	0	****	2.22	4. 4. 4. 4.	-	-
ACEI-SV	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
SV 14,288 **** **** **** **** 1.18 **** **** **	ACEI-SV	12,722	****	****	****	****	0.84	****	0.24	****	0.71 / 0.12 / 4.24)	0.700
Site-Adjusted Analysis ACEI-SV 13,667 ***** ***** ***** 2.14 ****** 2.14 ****** - </td <td>SV</td> <td>14,288</td> <td>****</td> <td>****</td> <td>****</td> <td>****</td> <td>1.18</td> <td>****</td> <td>-0.34</td> <td></td> <td>0.71 (0.12, 4.24)</td> <td>0.706</td>	SV	14,288	****	****	****	****	1.18	****	-0.34		0.71 (0.12, 4.24)	0.706
ACEI-SV 13,667 **** **** **** **** 2.14 **** 2.14 **** 5V 8,126 **** **** **** **** **** 0 ***** 0 ***** 5V 8,126 **** **** **** **** 0 ***** 0 ***** 5V 2,209 **** **** **** **** 0 ***** 0 ***** 0 ***** 0 ***** 5V 2,209 **** **** **** **** 0 ***** 0 ***** 0 ***** 0 ***** 1.92 ***** 1.9						181	- 270 Days					
SV 8,126 **** **** **** **** **** 0 ***** 2.14 *****	Site-Adjusted Analy	sis										
SV 8,126 **** **** **** **** 0 ***** 2.14 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 2,209 **** **** ***** 0 ***** 0 ***** SV 2,209 **** **** **** 0 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 7,751 **** **** ***** 1.92 *****	ACEI-SV	13,667	****	****	****	****	2.14	****	2.14	****		
ACEI-SV 2,209 **** **** **** **** 0 ***** 0 ***** 0 *****	SV	8,126	****	****	****	****	0	****	2.14		<u>-</u>	
ACEI-SV 2,209 **** **** **** **** 0 ***** 0 ***** 0 *****	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
SV 2,209 ***** ***** ***** 0 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 7,751 ***** ***** ***** 1.92 ***** 1.92 ***** 1.92 ***** -							0	****	0	****		
ACEI-SV 7,751 ***** ***** ***** 1.92 ***** 1.92 *****	SV	2,209	****	****	****	****	0	****	U	ren ren ren ren	-	-
ACEI-5V 7,751 1.92 1.92 *****	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
	ACEI-SV	7,751	****	****	****	****	1.92	****	1.02	****		
	SV	7,921	****	****	****	****	0	****	1.92		-	-

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

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) ¹	Wald P-Value ¹
					271	- 365 Days					
Site-Adjusted Analys	sis										
ACEI-SV	9,609	****	****	****	****	1.88	****	0.05	****	1 07 / 0 22 17 64)	0.544
SV	5,092	****	****	****	****	0.93	****	0.95		1.97 (0.22, 17.64)	0.544
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV	989	****	****	****	****	10.84	****	40.04	****		
SV	989	****	****	****	****	0	****	10.84	4.4.4.4.4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV	5,248	****	****	****	****	2.63	****		****	2.71 / 0.20, 20 10\	0.207
SV	4,991	****	****	****	****	0.94	****	1.69	4. 4. 4. 4. 4.	2.71 (0.28, 26.10)	0.387

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 8. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
						Overall					
Site-Adjusted Analys											
ARB-SV	48,455	****	****	****	****	2.62	****	1.33	****	2.10 (1.24, 3.57)	0.006
SV	43,845	****	****	****	****	1.28	****				
Fixed Ratio 1:1 Prop											
ARB-SV	37,893	****	****	****	****	4.02	****	2.44	****	2.55 (1.27, 5.11)	0.009
SV	37,893	****	****	****	****	1.58	****	2.77		2.55 (1.27, 5.11)	
Fixed Ratio 1:1 Prop	-			-	-						
ARB-SV	37,893	****	****	****	****	2.76	*****	1.38	****	2.03 (1.16, 3.54)	0.013
SV	37,893	****	****	****		1.38	****				
Cita Adimetad Amalo	-•-				0	- 30 Days					
Site-Adjusted Analys ARB-SV		****	****	****	****	3.88	****				
SV	48,455 43,845	****	****	****	****	3.88 1.15	****	2.73	****	3.36 (1.11, 10.22)	0.033
						1.15					
Fixed Ratio 1:1 Prop		****	****	****	*****	4.02	****				
ARB-SV SV	37,893	****	****	****	****	4.03	****	2.56	****	2.75 (0.88, 8.64)	0.083
Fixed Ratio 1:1 Prop	37,893					1.46					
ARB-SV	37,893	****	****	****	****	3.9	****				
SV	37,893	****	****	****	****	1.33	****	2.57	****	2.93 (0.93, 9.20)	0.066
3.0	37,633				31	- 60 Days					
Site-Adjusted Analys	sis					, ,					
ARB-SV	38,929	****	****	****	****	3.02	****	4.50	****	2.22 / 2.52 . 5.55	0.057
SV	39,911	****	****	****	****	1.49	****	1.53	****	2.00 (0.60, 6.65)	0.257
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	27,896	****	****	****	****	4.38	****	2.5	****	2.22 / 0.60 . 0.02)	0.22
SV	27,896	****	****	****	****	1.88	****	2.5	~ ~ ~ ~ ~	2.33 (0.60, 9.02)	0.22
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	30,495	****	****	****	****	3.38	****	1.66	****	1.97 (0.58, 6.72)	0.281
SV	34,703	****	****	****	****	1.71	****	1.00		1.37 (0.38, 0.72)	0.281

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Table 8. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys											
ARB-SV	26,362	****	****	****	****	3.57	****	1.53	****	1.79 (0.52, 6.14)	0.354
SV	26,165	****	****	****	****	2.04	****				
Fixed Ratio 1:1 Prop											
ARB-SV	12,369	****	****	****	****	7.11	****	4.74	****	3.00 (0.61, 14.86)	0.178
SV	12,369	****	****	****	****	2.37	****				
Fixed Ratio 1:1 Prop	<u> </u>	tched Unco	nditional A	nalysis; Cal	iper= 0.05 ****		****				
ARB-SV	20,601	****	*****	****	****	3.92	****	1.59	****	1.71 (0.48, 6.07)	0.405
SV	22,846	****	****	****		2.33	****			, ,	
Site-Adjusted Analys	cic .				91	- 180 Days					
ARB-SV	21,280	****	****	****	****	2.24	****				
SV	21,227	****	****	****	****	1.61	****	0.63	****	1.43 (0.51, 4.05)	0.496
Fixed Ratio 1:1 Prop		tched Conc	litional Ana	lvsis: Caline	r= 0.05 ²	1.01					
ARB-SV	8,114	****	****	*****	****	2.66	****				
SV	8,114	****	****	****	****	1.77	****	0.89	****	1.50 (0.25, 8.98)	0.657
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalvsis: Cal	iper= 0.05	1.77					
ARB-SV	16,557	****	****	****	****	2.25	****		ale ale ale ale		
SV	18,643	****	****	****	****	1.52	****	0.73	****	1.46 (0.46, 4.60)	0.518
	,				181	- 270 Days					
Site-Adjusted Analys	sis										
ARB-SV	13,053	****	****	****	****	1.51	****	1.06	****	3.25 (0.36, 29.12)	0.291
SV	11,473	****	****	****	****	0.45	****	1.00		3.23 (0.30, 29.12)	0.291
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	2,718	****	****	****	****	2.24	****	2.24	****		
SV	2,718	****	****	****	****	0	****	2.24			
Fixed Ratio 1:1 Prop					•						
ARB-SV	10,071	****	****	****	****	1.97	****	1.47	****	3.89 (0.43, 34.76)	0.225
SV	10,185	****	****	****	****	0.5	****	1.7/		3.03 (0.73, 37.70)	0.223

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Table 8. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					271	- 365 Days					
Site-Adjusted Analy	sis										
ARB-SV	8,961	****	****	****	****	1.03	****	0.37	****	1.50 (0.14, 16.58)	0.739
SV	7,184	****	****	****	****	0.66	****	0.57		1.50 (0.14, 16.56)	0.739
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	1,204	****	****	****	****	0	****	0	****		
SV	1,204	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	6,844	****	****	****	****	0.68	****	0.05	****	0.02 / 0.06 14 70)	0.056
SV	6,480	****	****	****	****	0.72	****	-0.05		0.92 (0.06, 14.79)	0.956

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
No Angioedema (-1	83, -1)										
	•					Overall					
Site-Adjusted Analy		****	****	****	****	2.26	****				
ARB-SV	48,399	****	****	****	****	2.26	****	1.23	****	2.26 (1.26, 4.05)	0.006
SV	43,786					1.03	7-1-1-1-1				
Fixed Ratio 1:1 Prop											
ARB-SV	37,832	****	****	****	****	3.3	****	2.01	****	2.56 (1.18, 5.52)	0.017
SV	37,832		****	****	*****	1.29	****			(-, ,	
Fixed Ratio 1:1 Prop		tched Unco	onditional A	nalysis; Cal	iper= 0.05 ****		****				
ARB-SV	37,832	****	****	****	****	2.38	****	1.29	****	2.20 (1.19, 4.08)	0.012
SV	37,832	****	****	****		1.1	*****			, , ,	
C': A !:	•				U	- 30 Days					
Site-Adjusted Analy		****	****	****	****		****				
ARB-SV	48,399	****	****	****	****	2.5	****	1.92	****	4.39 (0.95, 20.33)	0.059
SV	43,786					0.58	****			• • •	
Fixed Ratio 1:1 Prop		tched Con	ditional Ana								
ARB-SV	37,832	****	****	****	****	2.57	****	1.83	****	3.50 (0.73, 16.85)	0.118
SV	37,832	****	****	****	****	0.73	****				
Fixed Ratio 1:1 Prop					•						
ARB-SV	37,832	****	****	****	****	2.48	****	1.82	****	3.76 (0.78, 18.09)	0.099
SV	37,832	****	****	****	****	0.67	****			- 3 (,,,	
					31	60 Days					
Site-Adjusted Analy											
ARB-SV	38,888	****	****	****	****	3.02	****	1.53	****	2.00 (0.60, 6.65)	0.257
SV	39,859	****	****	****	****	1.49	****			=:== (3:33, 3:33)	0.20.

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Table 9. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	27,861	****	****	****	****	4.38	****	2.5	****	2.22 / 0.60 . 0.02)	0.22
SV	27,861	****	****	****	****	1.88	****	2.5	4. 4. 4. 4. 4.	2.33 (0.60, 9.02)	0.22
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	30,449	****	****	****	****	3.38	****	1.67	****	1.07/0.50 6.73\	0.281
SV	34,650	****	****	****	****	1.71	****	1.07		1.97 (0.58, 6.72)	0.281
					61	- 90 Days					
Site-Adjusted Analys	sis										
ARB-SV	26,334	****	****	****	****	3.06	****	1.53	****	1.96 (0.49, 7.85)	0.34
SV	26,128	****	****	****	****	1.53	****	1.55		1.90 (0.49, 7.65)	0.54
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	12,358	****	****	****	****	5.94	****	2.56	****	2.50 / 0.40 .42.00\	0.272
SV	12,358	****	****	****	****	2.37	****	3.56		2.50 (0.49, 12.89)	0.273
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	20,567	****	****	****	****	3.28	****	4.52	****	4.05 / 0.44 7.72)	0.404
SV	22,808	****	****	****	****	1.75	****	1.53	4. 4. 4. 4. 4.	1.85 (0.44, 7.73)	0.401
					91	- 180 Days					
Site-Adjusted Analys	sis										
ARB-SV	21,256	****	****	****	****	2.25	****	0.9	****	1.73 (0.58, 5.20)	0.326
SV	21,197	****	****	****	****	1.34	****	0.9		1.73 (0.36, 3.20)	0.520
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	8,097	****	****	****	****	2.66	****	0.00	****	4.50 / 0.35 . 0.63	0.657
SV	8,097	****	****	****	****	1.78	****	0.89	***	1.50 (0.25, 8.98)	0.657
Fixed Ratio 1:1 Prop		tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	16,526	****	****	****	****	2.26	****				
SV	18,613	****	****	****	****	1.22	****	1.04	****	1.83 (0.54, 6.25)	0.336

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Table 9. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
					181	- 270 Days					
Site-Adjusted Analy	sis										
ARB-SV	13,041	****	****	****	****	1.51	****	1.06	****	3.25 (0.36, 29.11)	0.291
SV	11,456	****	****	****	****	0.45	****	1.00		3.23 (0.30, 23.11)	0.231
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	2,716	****	****	****	****	2.24	****	2.24	****		
SV	2,716	****	****	****	****	0	****	2.24	40 40 40 40	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	10,057	****	****	****	****	1.97	****	4.47	****	2.00 / 0.42 24.76\	0.225
SV	10,168	****	****	****	****	0.5	****	1.47	40 40 40 40	3.88 (0.43, 34.76)	0.225
					271	- 365 Days					
Site-Adjusted Analy	sis										
ARB-SV	8,952	****	****	****	****	1.03	****	0.27	****	4.50/0.44.46.57\	0.74
SV	7,173	****	****	****	****	0.66	****	0.37	40 40 40 40	1.50 (0.14, 16.57)	0.74
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Calipe	er= 0.05 ²						
ARB-SV	1,209	****	****	****	****	0	****		****		
SV	1,209	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	6,834	****	****	****	****	0.68	****	0.05	****	0.02 / 0.00 14.70\	0.056
SV	6,468	****	****	****	****	0.72	****	-0.05	40 40 40 40	0.92 (0.06, 14.78)	0.956
Angioedema (-183,											
						Overall					
Site-Adjusted Analy	sis										
ARB-SV	56	****	****	****	****	333.33	****	156 10	****	164/046 504\	0.444
SV	59	****	****	****	****	177.15	****	156.19	ren ren ren ren	1.64 (0.46, 5.84)	0.444



Table 9. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1.000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
						Tears	New Osers	Tears	New Osers	ilitervalj	r-value
Fixed Ratio 1:1 Prop	36	****	*****	*****	*****	663.35	****				
SV	36 36	****	****	****	****	331.67	****	331.67	****	2.00 (0.37, 10.92)	0.423
Fixed Ratio 1:1 Prop		tched Unc	anditional A	nalycic: Cal		551.07					
ARB-SV	36	****	*****	*****	*****	368.32	****				
SV	36	****	****	****	****	292.61	****	75.71	****	1.09 (0.27, 4.35)	0.907
34	30				0	- 30 Days					
Site-Adjusted Analy	sis					00 20.70					
ARB-SV	56	****	****	****	****	1,253.13	****		****	/	
SV	59	****	****	****	****	428.27	****	824.87	****	2.84 (0.55, 14.73)	0.213
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Calipe	r= 0.05 ²						
ARB-SV	36	****	****	****	****	1,666.67	****				
SV	36	****	****	****	****	833.33	****	833.33	****	2.00 (0.37, 10.92)	0.423
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	36	****	****	****	****	1,593.63	****	001.07	****	2 22 / 0 / 1 / 12 / 5	0.357
SV	36	****	****	****	****	701.75	****	891.87	4. 4. 4. 4. 4.	2.22 (0.41, 12.15)	0.357
					31	- 60 Days					
Site-Adjusted Analy	sis										
ARB-SV	44	****	****	****	****	0	****	0	****	_	_
SV	54	****	****	****	****	0	****	0			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	23	****	****	****	****	0	****	0	****		
SV	23	****	****	****	****	0	****	<u> </u>		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	27	****	****	****	****	0	****	0	****		
SV	32	****	****	****	****	0	****	U		-	-

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Table 9. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys	sis										
ARB-SV	31	****	****	****	****	413.22	****	84.28	****	1.05 (0.07, 16.78)	0.973
SV	41	****	****	****	****	328.95	****	04.20		1.03 (0.07, 10.78)	0.973
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	11	****	****	****	****	0	****	0	****		
SV	11	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	18	****	****	****	****	0	****	-571.43	****		
SV	24	****	****	****	****	571.43	****	-5/1.43		-	-
					91	- 180 Days					
Site-Adjusted Analys	sis										
ARB-SV	27	****	****	****	****	0	****	-155.52	****		
SV	34	****	****	****	****	155.52	****	-133.32		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	17	****	****	****	****	0	****	290.0	****		
SV	19	****	****	****	****	280.9	****	-280.9		-	-
					181	- 270 Days					
Site-Adjusted Analy	sis										
ARB-SV	13	****	****	****	****	0	****	0	****		
SV	21	****	****	****	****	0	****	U		-	-



Table 9. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²					•	
ARB-SV SV	****	****	*****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV SV	11 11	*****	*****	*****	****	0 0	****	0	****	-	-
					271	- 365 Days					
Site-Adjusted Analys	sis										
ARB-SV SV	11 14	*****	*****	*****	*****	0 0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	and the site of the	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV SV	****	****	*****	*****	*****	0 0	****	0	****	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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	Average		Incidence Rate per		Incidence Rate Difference	Difference in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Unknown											
						Overall					
Site-Adjusted Analy	sis										
ARB-SV	7,859	****	****	****	****	1.51	****	0.75	****	2.31 (0.41, 12.85)	0.34
SV	7,214	****	****	****	****	0.75	****	0.75		2.31 (0.41, 12.03)	0.54
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	5,722	****	****	****	****	1.91	****	1.91	****	_	_
SV	5,722	****	****	****	****	0	****	1.91		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	5,722	****	****	****	****	1.03	****	0.57	****	2.43 (0.22, 26.98)	0.469
SV	5,722	****	****	****	****	0.46	****	0.57		2.43 (0.22, 20.98)	0.409
					0	- 30 Days					
Site-Adjusted Analy	sis										
ARB-SV	7,859	****	****	****	****	3.5	****	3.5	****	_	_
SV	7,214	****	****	****	****	0	****	3.3			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	5,722	****	****	****	****	2.49	****	2.40	****		
SV	5,722	****	****	****	****	0	****	2.49		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	5,722	****	****	****	****	2.4	****	2.4	****		
SV	5,722	****	****	****	****	0	****	2.4		-	-
					31	- 60 Days					
Site-Adjusted Analy	sis										
ARB-SV	6,039	****	****	****	****	0	****		****		
SV	6,505	****	****	****	****	0	****	0	* * * * *	-	-

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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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Calipe	r= 0.05 ²					•	
ARB-SV	4,004	****	****	****	****	0	****		****		
SV	4,004	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	•	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	4,398	****	****	****	****	0	****	0	****		
SV	5,207	****	****	****	****	0	****	0	4.4.4.4.4	-	-
					61	- 90 Days					
Site-Adjusted Analy	sis										
ARB-SV	4,107	****	****	****	****	3.29	****	0.24	****	1.11 (0.07, 18.45)	0.943
SV	4,385	****	****	****	****	3.05	****	0.24		1.11 (0.07, 16.45)	0.945
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	1,829	****	****	****	****	8.04	****	0.04	****		
SV	1,829	****	****	****	****	0	****	8.04	4.4.4.4.4	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	3,001	****	****	****	****	4.5	****	0.73	****	1 22 / 0 00 21 10)	0.045
SV	3,524	****	****	****	****	3.77	****	0.72		1.32 (0.08, 21.19)	0.845
					91	- 180 Days					
Site-Adjusted Analy	sis										
ARB-SV	3,285	****	****	****	****	1.57	****	0.02	****	1.51 (0.09, 24.24)	0.769
SV	3,544	****	****	****	****	1.55	****	0.02		1.51 (0.05, 24.24)	0.703
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	1,203	****	****	****	****	0	****	0	****		
SV	1,203	****	****	****	****	0	****	0	4-4-4-4-4-	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	2,412	****	****	****	****	0	****	_	ale ale ale ale		
SV	2,870	****	****	****	****	0	****	0	****	-	-



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) ¹	Wald P-Value ¹
					181	- 270 Days				•	
Site-Adjusted Analy	sis										
ARB-SV	2,082	****	****	****	****	0	****	0	****		
SV	2,021	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	448	****	****	****	****	0	****	0	****		
SV	448	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV	1,531	****	****	****	****	0	****	0	****		
SV	1,666	****	****	****	****	0	****	U		-	
					271	- 365 Days					
Site-Adjusted Analys	sis										
ARB-SV	1,422	****	****	****	****	0	****	0	****	_	_
SV	1,284	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	208	****	****	****	****	0	****	0	****	_	
SV	208	****	****	****	****	0	****	0		_	
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ARB-SV	1,039	****	****	****	****	0	****	0	****	_	_
SV	1,075	****	****	****	****	0	****				
Race: American Indi	ian										
						Overall					
Site-Adjusted Analy											
ARB-SV	128	****	****	****	****	0	****	0	****	_	_
SV	144	****	****	****	****	0	****	U		-	-

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						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop											
ARB-SV	95	****	****	****	****	0	****	_	****		
SV	95	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	95	****	****	****	****	0	****	0	****		
SV	95	****	****	****	****	0	****	0		-	-
					0	- 30 Days					
Site-Adjusted Analy	sis										
ARB-SV	128	****	****	****	****	0	****	0	****	_	_
SV	144	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	95	****	****	****	****	0	****	0	****		
SV	95	****	****	****	****	0	****			<u> </u>	
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ARB-SV	95	****	****	****	****	0	****	0	****	_	_
SV	95	****	****	****	****	0	****				
					31	- 60 Days					
Site-Adjusted Analy		4.4.4.4.	de de de de de	de de de de de	4.4.4.4.4		distributed.				
ARB-SV	99	****	****	****	****	0	****	0	****	-	-
SV	128	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop											
ARB-SV	66	****	****	****	****	0	****	0	****	-	_
SV	66	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	•				•		distributed.				
ARB-SV	73	****	****	****	****	0	****	0	****	-	-
SV	85	****	****	****	****	0	****	J			

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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) ¹	Wald P-Value ¹
					61	90 Days				,	
Site-Adjusted Analy	sis										
ARB-SV	63	****	****	****	****	0	****	0	****		
SV	86	****	****	****	****	0	****	0			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	33	****	****	****	****	0	****	0	****		
SV	33	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV	51	****	****	****	****	0	****	0	****		
SV	57	****	****	****	****	0	****	U		-	-
					91	- 180 Days					
Site-Adjusted Analy	sis										
ARB-SV	54	****	****	****	****	0	****	0	****	_	
SV	66	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	25	****	****	****	****	0	****	0	****		
SV	25	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV	45	****	****	****	****	0	****	0	****		
SV	49	****	****	****	****	0	****	0			_
					181	270 Days					
Site-Adjusted Analy											
ARB-SV	34	****	****	****	****	0	****	0	****	_	_
SV	32	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	<u> </u>		<u>-</u>	<u> </u>
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05	_	_		_		
ARB-SV	28	****	****	****	****	0	****	0	****		
SV	26	****	****	****	****	0	****	U		-	-

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Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events 271	Incidence Rate per 1,000 Person Years - 365 Days	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) ¹	Wald P-Value ¹
Site-Adjusted Analy	sis										
ARB-SV SV	23 18	****	*****	****	****	0 0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV SV	****	*****	*****	*****	*****	0 0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV SV Race: Asian	18 14	****	****	****	****	0 0	****	0	****	-	-
						Overall					
Site-Adjusted Analy	sis										
ARB-SV SV	1,055 525	****	*****	****	****	2.92 0	****	2.92	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV SV	475 475	****	*****	*****	*****	11.79 0	****	11.79	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV SV	475 475	*****	*****	*****	*****	6.44 0	****	6.44	****	-	-

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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) ¹	Wald P-Value ¹
					0	- 30 Days					
Site-Adjusted Analys		****	****	****	****		****				
ARB-SV	1,055	****	****	****	*****	0	****	0	****	-	-
SV	525					0	****				
Fixed Ratio 1:1 Prop		tched Cond	ditional Ana	lysis; Calipe ****							
ARB-SV	475		****	****	****	0	****	0	****	-	-
SV	475	*****				0	****				
Fixed Ratio 1:1 Prop	•	tcnea Unco	****	naiysis; Cali	*****	0	****				
ARB-SV	475	****	****	****	****	0	****	0	****	-	-
SV	475	4444	*****	*****		- 60 Days	4444				
Site-Adjusted Analys	sis				31	- 00 Days					
ARB-SV	776	****	****	****	****	0	****				
SV	483	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Conc	litional Ana	lysis: Caline	r= 0.05 ²						
ARB-SV	328	****	****	*****	****	0	****				
SV	328	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalvsis: Cali	per= 0.05						
ARB-SV	352	****	****	****	****	0	****		****		
SV	437	****	****	****	****	0	****	0	***	-	-
					61	- 90 Days					
Site-Adjusted Analys	sis					_					
ARB-SV	518	****	****	****	****	0	****	0	****		
SV	329	****	****	****	****	0	****	<u> </u>		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	147	****	****	****	****	0	****	0	****		
SV	147	****	****	****	****	0	****	0	ner ner ner ner	<u>-</u>	<u>-</u>
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ARB-SV	235	****	****	****	****	0	****	0	****		
SV	303	****	****	****	****	0	****	J		_	-

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Table 10. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

	Number of	Person Years	Average Person Days	Average Person Years	Number of	Rate per 1,000 Person	Risk per 1,000	Difference per 1,000 Person	in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
vicultai i i ouutt	ivew osers	at Misk	at Misk	at Nisk		- 180 Days	ivew Osers	rears	New Osers	intervary	r-value
Site-Adjusted Analy	sis										
ARB-SV	413	****	****	****	****	0	****		****		
SV	254	****	****	****	****	0	****	0	***	-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Calipe	r= 0.05 ²						
ARB-SV	92	****	****	****	****	0	****		****		
SV	92	****	****	****	****	0	****	0	****	-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ARB-SV	187	****	****	****	****	0	****	0	****		
SV	236	****	****	****	****	0	****	U		-	-
					181	- 270 Days					
Site-Adjusted Analy	sis										
ARB-SV	272	****	****	****	****	18.14	****	18.14	****	_	_
SV	138	****	****	****	****	0	****	10.14			
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	40	****	****	****	****	133.87	****	133.87	****	_	_
SV	40	****	****	****	****	0	****	133.67			
ixed Ratio 1:1 Prop	•				•						
ARB-SV	131	****	****	****	****	39.49	****	39.49	****	_	_
SV	129	****	****	****	****	0	****	33.43			
	-				271	- 365 Days					
ite-Adjusted Analy											
ARB-SV	184	****	****	****	****	0	****	0	****	-	_
	88	****	****	****	****	0	****				
SV	ensity Score Ma										
ixed Ratio 1:1 Prop		****	****	****	****	0	****	0	****	_	_
ixed Ratio 1:1 Prop ARB-SV	21										
ixed Ratio 1:1 Prop ARB-SV SV	21 21	****	****	****	****	0	****				
ixed Ratio 1:1 Prop ARB-SV	21 21	****				0	****				

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Table 10. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
						Overall				<u>, </u>	
Site-Adjusted Analys	sis										
ARB-SV	6,881	****	****	****	****	4.85	****	1 //2	****	1.42 (0.52, 3.93)	0.494
SV	5,888	****	****	****	****	3.44	****	1.42		1.42 (0.52, 3.93)	0.494
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	5,016	****	****	****	****	3.85	****	1 20	****	1 [0 / 0 3 [0 00)	0.657
SV	5,016	****	****	****	****	2.57	****	1.28	4.4.4.4.4	1.50 (0.25, 8.98)	0.657
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV	5,016	****	****	****	****	4.06	****	0.76	****	1.26 (0.38, 4.12)	0.707
SV	5,016	****	****	****	****	3.3	****	0.70		1.20 (0.36, 4.12)	0.707
					0	- 30 Days					
Site-Adjusted Analys	sis										
ARB-SV	6,881	****	****	****	****	5.88	****	3.73	****	2.62 (0.27, 25.23)	0.404
SV	5,888	****	****	****	****	2.14	****	3.73		2.02 (0.27, 23.23)	0.404
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	5,016	****	****	****	****	5.55	****	2.77	****	2.00 (0.18, 22.06)	0.571
SV	5,016	****	****	****	****	2.77	****	2.77		2.00 (0.18, 22.06)	0.571
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali							
ARB-SV	5,016	****	****	****	****	5.37	****	2.86	****	2.09 (0.19, 23.03)	0.548
SV	5,016	****	****	****	****	2.51	****	2.80		2.09 (0.19, 23.03)	0.548
					31	- 60 Days					
Site-Adjusted Analys	sis										
ARB-SV	5,477	****	****	****	****	5.6	****	2.67	****	1.96 (0.18, 21.58)	0.584
SV	5,357	****	****	****	****	2.93	****	2.07		1.55 (0.10, 21.50)	0.504
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	3,664	****	****	****	****	5.15	****	5.15	****	_	
SV	3,664	****	****	****	****	0	****	J.1J		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ARB-SV	4,003	****	****	****	****	3.84	****	0.44	****	1.13 (0.07, 18.12)	0.93
SV	4,589	****	****	****	****	3.41	****	U. 11		1.13 (0.07, 10.12)	0.33

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Table 10. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

Medical Product	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	Difference per 1,000 Person Years	in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ¹	Wald P-Value ¹
iviedicai Product	New Osers	at NISK	at NISK	at NISK		- 90 Days	New Osers	Tears	New Osers	intervaij	P-value
Site-Adjusted Analys	sis				- 01	30 Days					
ARB-SV	3,358	****	****	****	****	8.17	****				
SV	3,088	****	****	****	****	4.42	****	3.74	****	1.80 (0.16, 19.84)	0.633
ixed Ratio 1:1 Prop		tched Conc	litional Ana	lysis: Caline	r= 0.05 ²						
ARB-SV	1,291	****	****	****	****	0	****				
SV	1,291	****	****	****	****	11.78	****	-11.78	****	-	-
ixed Ratio 1:1 Prop		tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV	2,443	****	****	****	****	5.65	****	0.54	****	1 12 / 2 27 17 22)	2 2 2 2
SV	2,666	****	****	****	****	5.11	****	0.54	****	1.12 (0.07, 17.90)	0.936
	·				91	- 180 Days					
Site-Adjusted Analys	sis										
ARB-SV	2,565	****	****	****	****	2.18	****	-3.16	****	0.41 (0.04, 4.53)	0.468
SV	2,339	****	****	****	****	5.34	****	-3.10		0.41 (0.04, 4.53)	0.468
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	748	****	****	****	****	0	****	0	****		
SV	748	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ARB-SV	1,838	****	****	****	****	3.09	****	0.03	****	1.01 (0.06, 16.15)	0.994
SV	2,036	****	****	****	****	3.06	****	0.03		1.01 (0.00, 10.13)	0.334
					181	- 270 Days					
Site-Adjusted Analys											
ARB-SV	1,421	****	****	****	****	3.49	****	-1.47	****	0.73 (0.05, 11.69)	0.825
SV	1,062	****	****	****	****	4.96	****				
Fixed Ratio 1:1 Prop											
ARB-SV	206	****	****	****	****	0	****	0	****	_	_
SV	206	****	****	****	****	0	****				
ixed Ratio 1:1 Prop	•				•						
ARB-SV	995	****	****	****	****	4.97	****	-0.64	****	0.94 (0.06, 14.99)	0.964
SV	940	****	****	****	****	5.61 - 365 Days	****				

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Medical Product Site-Adjusted Analy	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) ¹	Wald P-Value ¹
ARB-SV	963	****	****	****	****	4.88	****	4.00	****		
SV	655	****	****	****	****	0	****	4.88	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	88	****	****	****	****	0	****	0	****		
SV	88	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	672	****	****	****	****	0	****				
SV	575	****	****	****	****	0	****	0	****	-	-

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Pacific Islande	er										
						Overall					
Site-Adjusted Analy											
ARB-SV	59	****	****	****	****	0	****	0	****	_	_
SV	44	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	34	****	****	****	****	0	****	0	****		
SV	34	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV	34	****	****	****	****	0	****	0	****		
SV	34	****	****	****	****	0	****	U		-	
					0	- 30 Days					
Site-Adjusted Analy	rsis										
ARB-SV	59	****	****	****	****	0	****	0	****		
SV	44	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	34	****	****	****	****	0	****	0	****		
SV	34	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV	34	****	****	****	****	0	****	0	****		
SV	34	****	****	****	****	0	****	<u> </u>		<u>-</u>	
					31	- 60 Days					
Site-Adjusted Analy	rsis										
ARB-SV	51	****	****	****	****	0	****	0	****		
SV	41	****	****	****	****	0	****	U		-	-

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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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	28	****	****	****	****	0	****	0	****		
SV	28	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	29	****	****	****	****	0	****	0	****		
SV	33	****	****	****	****	0	****	0		-	
					61	- 90 Days					
Site-Adjusted Analy	sis										
ARB-SV	34	****	****	****	****	0	****	0	****	_	_
SV	26	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	15	****	****	****	****	0	****	0	****		
SV	15	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	16	****	****	****	****	0	****	0	****		
SV	21	****	****	****	****	0	****	0			
					91	- 180 Days					
Site-Adjusted Analy											
ARB-SV	23	****	****	****	****	0	****	0	****	_	_
SV	23	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****			<u> </u>	
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cal	•						
ARB-SV	11	****	****	****	****	0	****	0	****		
SV	20	****	****	****	****	0	****	U		-	_

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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) ¹	Wald P-Value ¹
					181	- 270 Days				,	
Site-Adjusted Analy	sis										
ARB-SV	14	****	****	****	****	0	****	0	****		
SV	14	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²	_					
ARB-SV	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV	****	****	****	****	****	0	****	0	****		
SV	12	****	****	****	****	0	****	0	****	-	-
					271	- 365 Days					
Site-Adjusted Analy	sis										
ARB-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	***	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	4-4-4-4-4	-	-
Race: White											
						Overall					
Site-Adjusted Analy	sis										
ARB-SV	32,473	****	****	****	****	2.48	****	1.38	****	2 22 / 1 10 / (57)	0.014
SV	30,030	****	****	****	****	1.1	****	1.38		2.33 (1.19, 4.57)	0.014

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Table 10. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop					er= 0.05 ²					,	
ARB-SV	25,922	****	****	****	****	4.44	****		4.4.4.4.		
SV	25,922	****	****	****	****	1.21	****	3.23	****	3.67 (1.49, 9.04)	0.005
Fixed Ratio 1:1 Prop		tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	25,922	****	****	****	****	2.93	****	4.70	****	2.62 (4.20 5.27)	0.007
SV	25,922	****	****	****	****	1.14	****	1.78	****	2.62 (1.30, 5.27)	0.007
	·				0	- 30 Days					
Site-Adjusted Analy	rsis										
ARB-SV	32,473	****	****	****	****	3.7	****	2.44	****	2.02 / 0.70 .10.04\	0.106
SV	30,030	****	****	****	****	1.26	****	2.44		2.93 (0.79, 10.84)	0.106
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	25,922	****	****	****	****	4.25	****	2.55	****	2.67 (2.74 . 40.05)	0.4.7
SV	25,922	****	****	****	****	1.59	****	2.66	****	2.67 (0.71, 10.05)	0.147
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	25,922	****	****	****	****	4.12	****	2.66	****	2.05 / 0.76 (0.74)	0.133
SV	25,922	****	****	****	****	1.46	****	2.66		2.85 (0.76, 10.74)	0.122
					31	- 60 Days					
Site-Adjusted Analy	rsis										
ARB-SV	26,489	****	****	****	****	3.3	****	1.68	****	2.07 (0.52, 8.28)	0.304
SV	27,401	****	****	****	****	1.62	****	1.00		2.07 (0.32, 0.20)	0.304
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	19,386	****	****	****	****	5.31	****	4.42	****	(00 / 0 72 40 04)	0.007
SV	19,386	****	****	****	****	0.89	****	4.43	4-4-4-4-4	6.00 (0.72, 49.84)	0.097
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	21,150	****	****	****	****	4.14	****	2.0	****	2 26 / 0 69 16 64	0.139
SV	23,783	****	****	****	****	1.24	****	2.9	ran ran ran ran ran	3.36 (0.68, 16.64)	0.138

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Table 10. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
					61	- 90 Days				•	
Site-Adjusted Analys	sis										
ARB-SV	18,288	****	****	****	****	2.93	****	1.47	****	2.02 (0.37, 11.04)	0.417
SV	18,258	****	****	****	****	1.45	****	1.47		2.02 (0.57, 11.04)	0.417
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV	8,987	****	****	****	****	6.46	****	4.85	****	4.00 (0.45, 35.79)	0.215
SV	8,987	****	****	****	****	1.62	****	4.65		4.00 (0.45, 35.79)	0.215
Fixed Ratio 1:1 Prop	ensity Score Ma		nditional A	nalysis; Cali	iper= 0.05						
ARB-SV	14,548	****	****	****	****	3.69	****	2.03	****	2.21 (0.40, 12.06)	0.36
SV	15,922	****	****	****	****	1.66	****	2.03		2.21 (0.40, 12.00)	0.50
					91	- 180 Days					
Site-Adjusted Analys											
ARB-SV	14,942	****	****	****	****	2.48	****	1.35	****	2.15 (0.56, 8.30)	0.268
SV	15,009	****	****	****	****	1.13	****				
Fixed Ratio 1:1 Prop		tched Cond	litional Ana		r= 0.05 ²						
ARB-SV	6,020	****	****	****	****	4.81	****	4.81	****	_	_
SV	6,020	****	****	****	****	0	****	4.01			
Fixed Ratio 1:1 Prop					•						
ARB-SV	11,819	****	****	****	****	2.7	****	1.41	****	2.09 (0.52, 8.35)	0.298
SV	13,166	****	****	****	****	1.29	****	1.71		2.03 (0.32, 0.33)	0.230
					181	- 270 Days					
Site-Adjusted Analys											
ARB-SV	9,236	****	****	****	****	1.07	****	1.07	****	-	-
SV	8,209	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop											
ARB-SV	2,003	****	****	****	****	0	****	0	****	-	-
SV	2,003	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	•				•						
ARB-SV	7,240	****	****	****	****	1.37	****	1.37	****	-	-
SV	7,263	****	****	****	****	0	****	,			

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Table 10. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
					271	- 365 Days					
Site-Adjusted Analys	sis										
ARB-SV	6,365	****	****	****	****	0.72	****	0.2	****	0.70 / 0.05 12.55	0.064
SV	5,135	****	****	****	****	0.92	****	-0.2		0.78 (0.05, 12.55)	0.864
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV	899	****	****	****	****	0	****	6.00	****		
SV	899	****	****	****	****	6.08	****	-6.08	4.4.4.4.4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV	4,940	****	****	****	****	0.94	****	0.00	****	0.02 / 0.06 14.75\	0.055
SV	4,627	****	****	****	****	1.01	****	-0.08		0.92 (0.06, 14.75)	5) 0.955

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
						Overall				· ·	
Site-Adjusted Analy	sis										
ACEI-SV 14-day	48,920	****	****	****	****	2.44	****	-0.84	****	0.75 / 0.40 1.17\	0.208
ARB-SV 14-day	35,084	****	****	****	****	3.28	****	-0.84		0.75 (0.48, 1.17)	0.208
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	33,383	****	****	****	****	3.78	****	-0.94	****	0.90 (0.44 1.44)	0.457
ARB-SV 14-day	33,383	****	****	****	****	4.72	****	-0.94		0.80 (0.44, 1.44)	0.457
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	33,383	****	****	****	****	2.63	****	-0.61	****	0.81 (0.50, 1.33)	0.405
ARB-SV 14-day	33,383	****	****	****	****	3.24	****	-0.01		0.81 (0.30, 1.33)	0.403
					0	- 30 Days					
Site-Adjusted Analy											
ACEI-SV 14-day	48,920	****	****	****	****	3.94	****	-1.17	****	0.77 (0.36, 1.64)	0.495
ARB-SV 14-day	35,084	****	****	****	****	5.11	****				
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV 14-day	33,383	****	****	****	****	5.1	****	-0.46	****	0.92 (0.40, 2.08)	0.835
ARB-SV 14-day	33,383	****	****	****	****	5.57	****	-0.40		0.52 (0.40, 2.00)	0.033
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	33,383	****	****	****	****	5.38	****	0.43	****	1.09 (0.50, 2.38)	0.835
ARB-SV 14-day	33,383	****	****	****	****	4.94	****	0.43			
					31	- 60 Days					
Site-Adjusted Analy		de de de de de	de de de de d	de de de de d	4.4.4.4						
ACEI-SV 14-day	37,299	****	****	****	****	3.96	****	0.09	****	1.03 (0.39, 2.70)	0.954
ARB-SV 14-day	26,670	****	****	****	****	3.87	****			()	

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Table 11. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prope						Tears	New Osers	Tears	New Osers	intervaij	P-value
ACEI-SV 14-day	19,392	****	*****	****	****	3.59	****				
ARB-SV 14-day	19,392	****	****	****	****	5.59 4.49	****	-0.9	****	0.80 (0.21, 2.98)	0.739
Fixed Ratio 1:1 Prope		tched Unco	nditional A	nalysis: Cali	iner= 0.05	4.43					
ACEI-SV 14-day	25,261	****	****	****	****	3.5	****				
ARB-SV 14-day	25,535	****	****	****	****	3.46	****	0.05	****	1.01 (0.33, 3.14)	0.985
7.11.2 0 7 2 7 0 0 0 7					61	- 90 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day	25,081	****	****	****	****	2.7	****	1.00	****	0.72 / 0.24 .2.47\	0.507
ARB-SV 14-day	17,938	****	****	****	****	3.78	****	-1.08	4. 4. 4. 4. 4.	0.72 (0.21, 2.47)	0.597
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	8,804	****	****	****	****	0	****	2.44	****		
ARB-SV 14-day	8,804	****	****	****	****	3.41	****	-3.41	****	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	16,973	****	****	****	****	1.6	****	-2.33	****	0.41 / 0.00 3.10\	0.202
ARB-SV 14-day	17,220	****	****	****	****	3.93	****	-2.33		0.41 (0.08, 2.10)	0.282
					91	- 180 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day	19,871	****	****	****	****	0.78	****	-1.79	****	0.31 (0.08, 1.18)	0.086
ARB-SV 14-day	14,260	****	****	****	****	2.57	****	-1.79		0.31 (0.00, 1.10)	0.080
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	5,539	****	****	****	****	2.38	****	-1.19	****	0.67 (0.11, 3.99)	0.657
ARB-SV 14-day	5,539	****	****	****	****	3.57	****	-1.19		0.07 (0.11, 3.99)	0.037
Fixed Ratio 1:1 Prope											
ACEI-SV 14-day	13,385	****	****	****	****	1.16	****	-1.51	****	0.43 (0.11, 1.67)	0.224
ARB-SV 14-day	13,703	****	****	****	****	2.67	****	-1.51		0.73 (0.11, 1.07)	0.224
					181	- 270 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	12,720	****	****	****	****	1.91	****	-0.28	****	0.90 (0.24, 3.35)	0.875
ARB-SV 14-day	8,967	****	****	****	****	2.19	****	0.20		0.50 (0.24, 5.55)	0.073

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Table 11. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day ARB-SV 14-day	2,226 2,226	*****	*****	*****	****	7.77 7.77	****	0	****	1.00 (0.20, 4.95)	1
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day ARB-SV 14-day	8,531 8,631	*****	*****	*****	****	2.86 2.27	*****	0.59	****	1.27 (0.34, 4.72)	0.724
					271	- 365 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day ARB-SV 14-day	9,007 6,248	*****	*****	*****	*****	1.5 1.47	****	0.03	****	1.03 (0.17, 6.15)	0.977
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	1,131	****	****	****	****	0	****	0	****		
ARB-SV 14-day	1,131	****	****	****	****	0	****	0		<u>-</u>	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day ARB-SV 14-day	5,967 6,021	****	*****	****	*****	0 1.53	****	-1.53	****	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 12. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, 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 Risk Window

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) ¹	Wald P-Value ¹
No Angioedema (-18		at Misk	at Misk	at mak	LVEIICS	i cai s	14CW 03CI3	icais	14EW 03EIS	intervary	1-Value
	, -,					Overall					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	48,874	****	****	****	****	2.38	****	0.56	****	0.02 (0.52 . 4.20)	0.202
ARB-SV 14-day	35,051	****	****	****	****	2.94	****	-0.56	75 75 75 75 75	0.82 (0.52, 1.30)	0.393
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	33,350	****	****	****	****	3.78	****	0.20	****	0.04 / 0.50 .4.67\	0.750
ARB-SV 14-day	33,350	****	****	****	****	4.16	****	-0.38	****	0.91 (0.50, 1.67)	0.758
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	33,350	****	****	****	****	2.63	****	-0.34	****	0.90 / 0.54 1.46)	0.627
ARB-SV 14-day	33,350	****	****	****	****	2.97	****	-0.34		0.89 (0.54, 1.46)	0.637
					0	- 30 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	48,874	****	****	****	****	3.94	****	0.4	****	1.11 (0.48, 2.56)	0.811
ARB-SV 14-day	35,051	****	****	****	****	3.54	****	0.4		1.11 (0.40, 2.30)	0.011
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	33,350	****	****	****	****	5.11	****	0.93	****	1.22 (0.51, 2.95)	0.655
ARB-SV 14-day	33,350	****	****	****	****	4.18	****	0.33		1.22 (0.31, 2.93)	0.033
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	33,350	****	****	****	****	5.38	****	1.67	****	1.45 (0.62, 3.39)	0.391
ARB-SV 14-day	33,350	****	****	****	****	3.71	****	1.07		1.43 (0.02, 3.33)	0.551
					31	60 Days					
Site-Adjusted Analy	sis					<u> </u>	<u> </u>	<u> </u>	<u> </u>		<u> </u>
ACEI-SV 14-day	37,263	****	****	****	****	3.56	****	-0.31	****	0.92 (0.34, 2.48)	0.877
ARB-SV 14-day	26,649	****	****	****	****	3.87	****	-0.51		0.32 (0.34, 2.40)	0.077

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Table 12. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average				Difference	in		
		Davasa	Average	Average	Neuralian	Rate per	Diale man			Hazard Ratio	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per		Wald
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	19,382	****	****	****	****	3.59	****	-0.9	****	0.80 (0.21, 2.98)	0.739
ARB-SV 14-day	19,382	****	****	****	****	4.49	****	-0.9		0.60 (0.21, 2.96)	0.739
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	25,235	****	****	****	****	3.51	****	0.05	****	1.01 (0.33, 3.14)	0.984
ARB-SV 14-day	25,514	****	****	****	****	3.46	****	0.03		1.01 (0.33, 3.14)	0.364
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	25,060	****	****	****	****	2.7	****	-1.08	****	0.72 (0.21, 2.47)	0.597
ARB-SV 14-day	17,924	****	****	****	****	3.78	****	-1.00		0.72 (0.21, 2.47)	0.557
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	8,797	****	****	****	****	0	****	-3.41	****		
ARB-SV 14-day	8,797	****	****	****	****	3.41	****	-3.41		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	16,955	****	****	****	****	1.6	****	-2.33	****	0.41 (0.08, 2.10)	0.282
ARB-SV 14-day	17,204	****	****	****	****	3.93	****	-2.55		0.41 (0.08, 2.10)	0.262
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	19,858	****	****	****	****	0.78	****	-1.79	****	0.31 (0.08, 1.18)	0.086
ARB-SV 14-day	14,248	****	****	****	****	2.57	****	-1./9		0.51 (0.00, 1.10)	0.000
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	5,535	****	****	****	****	2.38	****	1 10	****	0.67 (0.11 - 2.00)	0.657
ARB-SV 14-day	5,535	****	****	****	****	3.57	****	-1.19		0.67 (0.11, 3.99)	0.657

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Table 12. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, 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 Risk Window

			Average	Average		Incidence Rate per		Incidence Rate Difference	Difference in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	•				•						
ACEI-SV 14-day	13,372	****	****	****	****	1.16	****	-1.51	****	0.43 (0.11, 1.67)	0.224
ARB-SV 14-day	13,691	****	****	****	****	2.68	****	1.51		0.43 (0.11, 1.07)	0.224
					181	- 270 Days					
Site-Adjusted Analysi	is										
ACEI-SV 14-day	12,710	****	****	****	****	1.91	****	-0.28	****	0.90 (0.24, 3.35)	0.874
ARB-SV 14-day	8,960	****	****	****	****	2.19	****	-0.28		0.90 (0.24, 3.33)	0.874
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	2,226	****	****	****	****	7.77	****	0	****	1.00 / 0.20 .4.05\	1
ARB-SV 14-day	2,226	****	****	****	****	7.77	****	U		1.00 (0.20, 4.95)	1
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	8,522	****	****	****	****	2.86	****	0.50	****	1 27 / 0 24 4 72)	0.724
ARB-SV 14-day	8,625	****	****	****	****	2.27	****	0.59		1.27 (0.34, 4.72)	0.724
					271	- 365 Days					
Site-Adjusted Analysi	is										
ACEI-SV 14-day	8,999	****	****	****	****	1.5	****	0.03	****	1.02 / 0.17 (5.14)	0.978
ARB-SV 14-day	6,241	****	****	****	****	1.47	****	0.03		1.03 (0.17, 6.14)	0.978
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	1,133	****	****	****	****	0	****		****		
ARB-SV 14-day	1,133	****	****	****	****	0	****	0	75 75 75 75 75	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	5,962	****	****	****	****	0	****	-1.53	****		
ARB-SV 14-day	6,016	****	****	****	****	1.53	****	-1.55		-	-

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Table 12. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, 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 Risk Window

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) ¹	Wald P-Value ¹
Angioedema (-183, -		at Misk	at Misk	at Misk	LVEIILS	Tears	New Osers	rears	New Osers	intervary	r-value
	_ -,					Overall					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	46	****	****	****	****	77.34	****	242.20	****	0.45 (0.02 , 4.52)	0.100
ARB-SV 14-day	33	****	****	****	****	390.63	****	-313.29	4. 4. 4. 4. 4.	0.15 (0.02, 1.52)	0.109
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	20	****	****	****	****	0	****	126.60	****		
ARB-SV 14-day	20	****	****	****	****	436.68	****	-436.68	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	20	****	****	****	****	0	****	145 56	****		
ARB-SV 14-day	20	****	****	****	****	145.56	****	-145.56		-	-
					0	- 30 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	46	****	****	****	****	0	****	-1851.85	****	_	_
ARB-SV 14-day	33	****	****	****	****	1,851.85	****	-1831.83			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	20	****	****	****	****	0	****	-746.27	****		
ARB-SV 14-day	20	****	****	****	****	746.27	****	-740.27		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	20	****	****	****	****	0	****	-729.93	****	_	_
ARB-SV 14-day	20	****	****	****	****	729.93	****	-723.33			
					31	- 60 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	38	****	****	****	****	392.16	****	392.16	****	_	_
ARB-SV 14-day	23	****	****	****	****	0	****	332.10			

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Table 12. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average				Difference	in		
		D	Average	Average	Necesia	Rate per	Diale man			Hazard Ratio	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	(95% Confidence	Wald
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	•	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	nsity Score Mat			lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	15	****	****	****	****	0	****	0	****		_
ARB-SV 14-day	15	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	17	****	****	****	****	0	****	0	****		_
ARB-SV 14-day	16	****	****	****	****	0	****	U		-	
					61	- 90 Days					
Site-Adjusted Analysi	S										
ACEI-SV 14-day	26	****	****	****	****	0	****	0	****		_
ARB-SV 14-day	14	****	****	****	****	0	****	0		_	
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	11	****	****	****	****	0	****	0	****	_	
ARB-SV 14-day	11	****	****	****	****	0	****	0		-	-
					91	- 180 Days					
Site-Adjusted Analysis	S										
ACEI-SV 14-day	18	****	****	****	****	0	****		****		
ARB-SV 14-day	12	****	****	****	****	0	****	0		<u>-</u>	
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						_
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0	nen nen nen nen	-	-

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Table 12. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0		-	-
					181	- 270 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day	14	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	U		-	-
					271	365 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day	13	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0	<i>ጉጉ ጥ ጥ</i>	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0	****	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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	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) ¹	Wald P-Value ¹
Race: Unknown	New Osers	at RISK	at RISK	at RISK	Events	Years	New Osers	rears	New Osers	intervaij	P-value
Nace. Officiowii						Overall					
Site-Adjusted Analy	sis					<u> </u>					
ACEI-SV 14-day	7,922	****	****	****	****	1.58	****			/	
ARB-SV 14-day	5,604	****	****	****	****	1.71	****	-0.13	****	0.86 (0.19, 3.87)	0.848
Fixed Ratio 1:1 Prop		tched Con	ditional Ana	lysis: Caline	r= 0.05 ²						
ACEI-SV 14-day	5.241	****	****	****	****	2.57	****				
ARB-SV 14-day	5,241	****	****	****	****	3.86	****	-1.29	****	0.67 (0.11, 3.99)	0.657
Fixed Ratio 1:1 Prop		tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	5,241	****	****	****	****	1.21	****	0.6	****	0.55 / 0.44 . 0.00	0.500
ARB-SV 14-day	5,241	****	****	****	****	1.81	****	-0.6	****	0.65 (0.11, 3.90)	0.638
•					0	- 30 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	7,922	****	****	****	****	1.79	****	2.20	****	0.35 / 0.03 .2.95\	0.388
ARB-SV 14-day	5,604	****	****	****	****	5.08	****	-3.29		0.35 (0.03, 3.85)	0.388
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	5,241	****	****	****	****	3.13	****	2.12	****	0.50/0.05 5.51	0.571
ARB-SV 14-day	5,241	****	****	****	****	6.26	****	-3.13		0.50 (0.05, 5.51)	0.571
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	5,241	****	****	****	****	2.72	****	-2.69	****	0.50 (0.05, 5.50)	0.57
ARB-SV 14-day	5,241	****	****	****	****	5.41	****	-2.09		0.30 (0.03, 3.30)	0.57
					31	60 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	5,650	****	****	****	****	2.59	****	2.59	****	_	_
ARB-SV 14-day	3,986	****	****	****	****	0	****	2.33			

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	2,660	****	****	****	****	6.42	****	6.42	****		
ARB-SV 14-day	2,660	****	****	****	****	0	****	0.42		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	3,695	****	****	****	****	3.94	****	3.94	****	_	_
ARB-SV 14-day	3,758	****	****	****	****	0	****	3.94		-	-
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	3,867	****	****	****	****	3.52	****	3.52	****	_	_
ARB-SV 14-day	2,678	****	****	****	****	0	****	3.32			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	1,257	****	****	****	****	0	****	0	****		
ARB-SV 14-day	1,257	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	2,538	****	****	****	****	0	****	0	****		
ARB-SV 14-day	2,530	****	****	****	****	0	****	U		-	-
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	3,028	****	****	****	****	0	****	-2.42	****	_	_
ARB-SV 14-day	2,116	****	****	****	****	2.42	****	-2.42			_
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	794	****	****	****	****	0	****	0.00	****		
ARB-SV 14-day	794	****	****	****	****	8.02	****	-8.02	nan nan nan nan	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	1,969	****	****	****	****	0	****	-2.54	****		
ARB-SV 14-day	2,012	****	****	****	****	2.54	****	-2.34		-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					181	270 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	1,954	****	****	****	****	0	****	0	****		
ARB-SV 14-day	1,357	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	341	****	****	****	****	0	****		****		
ARB-SV 14-day	341	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	1,268	****	****	****	****	0	****	0	****		
ARB-SV 14-day	1,290	****	****	****	****	0	****	0	4.4.4.4.4	-	-
					271	- 365 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	1,381	****	****	****	****	3.25	****	2.25	****		
ARB-SV 14-day	933	****	****	****	****	0	****	3.25		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	186	****	****	****	****	0	****		****		
ARB-SV 14-day	186	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	896	****	****	****	****	0	****	0	****		
ARB-SV 14-day	885	****	****	****	****	0	****	0	4.4.4.4.4	-	-
Race: American India	an										
						Overall					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	160	****	****	****	****	0	****	0	****		
ARB-SV 14-day	82	****	****	****	****	0	****	0		-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

	-							Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	72	****	****	****	****	0	****	0	****		
ARB-SV 14-day	72	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	72	****	****	****	****	0	****	0	****		
ARB-SV 14-day	72	****	****	****	****	0	****	0		-	-
					0	- 30 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	160	****	****	****	****	0	****	0	****		
ARB-SV 14-day	82	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	72	****	****	****	****	0	****	0	****		
ARB-SV 14-day	72	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	72	****	****	****	****	0	****	0	****		
ARB-SV 14-day	72	****	****	****	****	0	****	U		-	-
					31	60 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	121	****	****	****	****	0	****	0	****		_
ARB-SV 14-day	59	****	****	****	****	0	****	0		_	_
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	39	****	****	****	****	0	****	0	****		
ARB-SV 14-day	39	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	55	****	****	****	****	0	****	0	****		
ARB-SV 14-day	51	****	****	****	****	0	****	U		-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	77	****	****	****	****	0	****	0	****		
ARB-SV 14-day	34	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	17	****	****	****	****	0	****	0	****		
ARB-SV 14-day	17	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	34	****	****	****	****	0	****	0	****		
ARB-SV 14-day	28	****	****	****	****	0	****	0		-	
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	61	****	****	****	****	0	****	0	****		
ARB-SV 14-day	31	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	13	****	****	****	****	0	****	0	****		
ARB-SV 14-day	13	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	26	****	****	****	****	0	****	0	****		
ARB-SV 14-day	27	****	****	****	****	0	****	0	nan nan nan nan	-	-
					181	- 270 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	38	****	****	****	****	0	****	0	****		
ARB-SV 14-day	16	****	****	****	****	0	****	U		-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0	***	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	14	****	****	****	****	0	****	0	****		
ARB-SV 14-day	14	****	****	****	****	0	****	U		-	-
					271	365 Days					
Site-Adjusted Analysi	is										
ACEI-SV 14-day	28	****	****	****	****	0	****	0	****		
ARB-SV 14-day	11	****	****	****	****	0	****	0			
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	11	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0		_	_
Race: Asian											
						Overall					
Site-Adjusted Analysi											
ACEI-SV 14-day	525	****	****	****	****	0	****	-3.86	****	_	_
ARB-SV 14-day	847	****	****	****	****	3.86	****	-3.00			
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	455	****	****	****	****	0	****	0	****		
ARB-SV 14-day	455	****	****	****	****	0	****	0		-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence	D:11		
			_	_		Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	455	****	****	****	****	0	****	6.00	****		
ARB-SV 14-day	455	****	****	****	****	6.89	****	-6.89		-	-
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	525	****	****	****	****	0	****	0	****		
ARB-SV 14-day	847	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	455	****	****	****	****	0	****	0	****		
ARB-SV 14-day	455	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	455	****	****	****	****	0	****	0	****		
ARB-SV 14-day	455	****	****	****	****	0	****	0		-	-
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	380	****	****	****	****	0	****	0	****		
ARB-SV 14-day	587	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	247	****	****	****	****	0	****	0	****		
ARB-SV 14-day	247	****	****	****	****	0	****	0	4, 4, 4, 4, 4,	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	331	****	****	****	****	0	****	0	****		
ARB-SV 14-day	329	****	****	****	****	0	****	U	ran ran ran ran	-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days				,	
Site-Adjusted Analys	sis					-					
ACEI-SV 14-day	260	****	****	****	****	0	****	0	****		
ARB-SV 14-day	392	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	116	****	****	****	****	0	****	0	****		
ARB-SV 14-day	116	****	****	****	****	0	****	0	40 40 40 40	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	228	****	****	****	****	0	****	0	****		
ARB-SV 14-day	223	****	****	****	****	0	****	U		-	
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	195	****	****	****	****	0	****	0	****	_	_
ARB-SV 14-day	309	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	74	****	****	****	****	0	****	0	****		
ARB-SV 14-day	74	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	174	****	****	****	****	0	****	0	****	_	_
ARB-SV 14-day	180	****	****	****	****	0	****				
					181	- 270 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	135	****	****	****	****	0	****	-24.17	****	-	-
ARB-SV 14-day	207	****	****	****	****	24.17	****	,			

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

•		-					la d'alana			
					Incidence			Difference		
		Average	Average							
	Dorcon	_	•	Number	-	Dick nor			Hazard Ratio	
Nihanaf					-	-	•	-		Wald
		-		_		,		•	•	
					Years	New Users	Years	New Users	Interval) ⁻	P-Value ¹
ensity Score Ma										
34		****	****		0	****	Ω	****	_	_
34		****	****		0	****	0		_	
ensity Score Ma				•						
119	****	****	****	****	0	****	-42.54	****	_	_
118	****	****	****	****	42.54	****	-42.54		_	
				271	- 365 Days					
sis										
101	****	****	****	****	0	****	0	****		
134	****	****	****	****	0	****	U		-	-
ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
19	****	****	****	****	0	****	0	****		
19	****	****	****	****	0	****	U		-	-
ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
89	****	****	****	****	0	****	0	****		
73	****	****	****	****	0	****	U		-	-
					Overall					
sis										
5,967	****	****	****	****	6.92	****	1 70	****	1 20 / 0 52 - 2 45\	0.524
4,736	****	****	****	****	5.14	****	1./8	4, 4, 4, 4, 4,	1.30 (0.53, 3.45)	0.521
ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
4,255	****	****	****	****	10.41	****			0.00/0.64 44.55	2) 2.175
4,255	****	****	****	****	3.47	ale ale ale ale		* * * * *	3.00 (0.61, 14.86)	0.178
	34 34 34 31 ensity Score Mate 119 118 sis 101 134 ensity Score Mate 19 19 ensity Score Mate 89 73 sis 5,967 4,736 ensity Score Mate 4,255	New Users at Risk ensity Score Matched Conc 34 ***** 34 ***** ensity Score Matched Unco 119 ***** 118 ***** 101 ***** 134 ***** ensity Score Matched Conc 19 ***** 19 ***** ensity Score Matched Unco 89 ***** 73 ***** ensity Score Matched Unco 89 ***** ensity Score Matched Unco 89 ***** ensity Score Matched Unco 89 ***** ensity Score Matched Conc 4,736 ***** ensity Score Matched Conc 4,255 *****	Number of Years Days New Users at Risk at Risk ensity Score Matched Conditional Ana 34 ***** ***** ensity Score Matched Unconditional A 119 ***** ***** 118 ***** 101 ***** ***** 134 ***** ensity Score Matched Conditional Ana 19 ***** ***** ensity Score Matched Conditional Ana 19 ***** ***** ensity Score Matched Unconditional Ana 19 ***** ***** ensity Score Matched Unconditional Ana 89 ***** ***** 73 ***** ***** ensity Score Matched Unconditional Ana 4,736 ***** ***** ensity Score Matched Unconditional Ana 4,255 ***** *****	Number of Years Days Years New Users at Risk at Risk at Risk ensity Score Matched Conditional Analysis; Calipe 34 **** **** ***** 34 ***** **** ****	Person Person Person Number Number of Years Days Years Of New Users at Risk at Risk at Risk Events Events	Number of Years Days Years Of Person New Users at Risk at Risk at Risk Events Years Sensity Score Matched Conditional Analysis; Caliper= 0.05 ² 34	Number of Years Days Years Of Person Number 1,000 Risk per	Number of Person Person Person Person Number 1,000 Risk per person Person Number 1,000 Person New Users at Risk at Risk at Risk Events Years New Users New Users New Users Years New Users New U	Number of Person 1,000 Pe	Number of Person Person Person Person Person Number of Person Person Person Person Number of Number of Person Number of Number of Person Number of Number

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1.000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	` Interval)¹	P-Value ¹
Fixed Ratio 1:1 Prope											
ACEI-SV 14-day	4,255	****	****	****	****	8.11	****		****		
ARB-SV 14-day	4,255	****	****	****	****	4.06	****	4.05	****	2.01 (0.69, 5.87)	0.204
	·				0	- 30 Days					
Site-Adjusted Analysi	is										
ACEI-SV 14-day	5,967	****	****	****	****	13.97	****	5.17	****	1.61 (0.40, 6.44)	0.5
ARB-SV 14-day	4,736	****	****	****	****	8.8	****	5.17		1.01 (0.40, 0.44)	0.5
Fixed Ratio 1:1 Prope	ensity Score Mat	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	4,255	****	****	****	****	14.85	****	7.42	****	2.00 (0.37, 10.92)	0.423
ARB-SV 14-day	4,255	****	****	****	****	7.42	****	7.42		2.00 (0.57, 10.92)	0.423
Fixed Ratio 1:1 Prope	ensity Score Mat	tched Unco		nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	4,255	****	****	****	****	16.4	****	9.87	****	2.51 (0.49, 12.92)	0.272
ARB-SV 14-day	4,255	****	****	****	****	6.53	****	9.67		2.31 (0.49, 12.92)	0.272
					31	- 60 Days					
Site-Adjusted Analysi	is										
ACEI-SV 14-day	4,444	****	****	****	****	13.8	****	9.48	****	3.16 (0.35, 28.24)	0.304
ARB-SV 14-day	3,528	****	****	****	****	4.32	****	J.+0		3.10 (0.33, 20.24)	0.504
Fixed Ratio 1:1 Prope	ensity Score Mat	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	2,355	****	****	****	****	7.7	****	7.7	****		
ARB-SV 14-day	2,355	****	****	****	****	0	****	7.7		and the state of t	
Fixed Ratio 1:1 Prope	ensity Score Mat				•						
ACEI-SV 14-day	3,150	****	****	****	****	14.5	****	14.5	****	_	_
ARB-SV 14-day	3,171	****	****	****	****	0	****	14.5		_	_

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	2,740	****	****	****	****	0	****	-6.3	****		
ARB-SV 14-day	2,194	****	****	****	****	6.3	****	-0.5		-	_
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	960	****	****	****	****	0	****	0	****		
ARB-SV 14-day	960	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	1,978	****	****	****	****	0	****	C 07	****		
ARB-SV 14-day	1,983	****	****	****	****	6.97	****	-6.97		-	-
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	2,051	****	****	****	****	2.61	****	2.61	****		
ARB-SV 14-day	1,656	****	****	****	****	0	****	2.01		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	534	****	****	****	****	13.52	****	42.52	****		
ARB-SV 14-day	534	****	****	****	****	0	****	13.52	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	1,469	****	****	****	****	3.63	****	2.62	****		
ARB-SV 14-day	1,498	****	****	****	****	0	****	3.63		-	-
					181	- 270 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	1,235	****	****	****	****	4	****	1.2	****	0.76 / 0.05 12.15	0.846
ARB-SV 14-day	943	****	****	****	****	5.2	****	-1.2		0.76 (0.05, 12.15)	0.840

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Proper	nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	168	****	****	****	****	0	****	0	****		
ARB-SV 14-day	168	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Proper	nsity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	890	****	****	****	****	5.64	****	-0.06	****	0.99 (0.06, 15.82)	0.994
ARB-SV 14-day	860	****	****	****	****	5.7	****	-0.00		0.99 (0.00, 13.82)	0.554
					271	- 365 Days					
Site-Adjusted Analysis	s										
ACEI-SV 14-day	837	****	****	****	****	0	****	-7.12	****	_	_
ARB-SV 14-day	658	****	****	****	****	7.12	****	-7.12		<u>-</u>	
Fixed Ratio 1:1 Proper	nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	86	****	****	****	****	0	****	0	****		
ARB-SV 14-day	86	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Proper	nsity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	584	****	****	****	****	0	****	-7.77	****		
ARB-SV 14-day	601	****	****	****	****	7.77	****	-7.77		-	-
Race: Pacific Islander											
						Overall					
Site-Adjusted Analysis	S										
ACEI-SV 14-day	46	****	****	****	****	0	****	0	****	_	_
ARB-SV 14-day	45	****	****	****	****	0	****			<u>-</u>	
Fixed Ratio 1:1 Proper	nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	35	****	****	****	****	0	****	0	****		
ARB-SV 14-day	35	****	****	****	****	0	****	U		-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	35	****	****	****	****	0	****	0	****		
ARB-SV 14-day	35	****	****	****	****	0	****	0		-	-
					0 -	- 30 Days					
Site-Adjusted Analysis	s										
ACEI-SV 14-day	46	****	****	****	****	0	****	0	****		_
ARB-SV 14-day	45	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	35	****	****	****	****	0	****	0	****		
ARB-SV 14-day	35	****	****	****	****	0	****	0			
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	35	****	****	****	****	0	****	0	****		
ARB-SV 14-day	35	****	****	****	****	0	****	0		-	
					31	- 60 Days					
Site-Adjusted Analysis	s										
ACEI-SV 14-day	33	****	****	****	****	0	****	0	****		
ARB-SV 14-day	37	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	21	****	****	****	****	0	****	0	****		
ARB-SV 14-day	21	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	25	****	****	****	****	0	****	0	****		
ARB-SV 14-day	29	****	****	****	****	0	****	U		-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
iviedicai Product	New Osers	at Risk	at KISK	at RISK		- 90 Days	New Osers	rears	New Osers	intervaij	P-value
Site-Adjusted Analys	ric .				01	- 90 Days					
ACEI-SV 14-day	23	****	****	****	****	0	****				
ARB-SV 14-day	22	****	****	****	****	0	****	0	****	-	-
		4 - la - al - C - a -	l:4: l A		0.052	- 0					
Fixed Ratio 1:1 Prop	ensity Score Ma	*****	****	iysis; Calipe	er= 0.05 *****		****				
ACEI-SV 14-day			****		*****	0		0	****	-	_
ARB-SV 14-day	****	****		****		0	****				
Fixed Ratio 1:1 Prop	•				•						
ACEI-SV 14-day	17	****	****	****	****	0	****	0	****	_	_
ARB-SV 14-day	18	****	****	****	****	0	****				
					91 -	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	20	****	****	****	****	0	****	0	****		
ARB-SV 14-day	14	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-dav	****	****	****	****	****	0	****	_	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	14	****	****	****	****	0	****		****		
ARB-SV 14-day	11	****	****	****	****	0	****	0	****	-	-
					181	- 270 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	13	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0	and the state of	-	-

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0	4.4.4.4.4	-	-
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	U		-	-
					271	- 365 Days					
Site-Adjusted Analysis	s										
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
ARB-SV 14-day	****	****	****	****	****	0	****	U		-	_
Race: White											
						Overall					
Site-Adjusted Analysis	s										
ACEI-SV 14-day	34,300	****	****	****	****	2.02	****	-1.28	****	0.62 (0.36, 1.07)	0.084
ARB-SV 14-day	23,770	****	****	****	****	3.3	****	-1.20		0.02 (0.30, 1.07)	0.064
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	22,933	****	****	****	****	3.12	****	1.2	****	0.71 / 0.24 1.40\	0.250
ARB-SV 14-day	22,933	****	****	****	****	4.43	****	-1.3	ran ran ran ran	0.71 (0.34, 1.48)	0.356

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1.000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope						1 Cais	New Osers	ieais	New Osers	iiiteivaij	r-value
ACEI-SV 14-day	22,933	****	****	*****	****	2.17	****				
ARB-SV 14-day	22,933	****	****	****	****	3.28	****	-1.11	****	0.66 (0.36, 1.22)	0.183
7111D SV 14 day	22,333				0 -	- 30 Days					
Site-Adjusted Analysi	s										
ACEI-SV 14-day	34,300	****	****	****	****	2.78	****	4.04	****	0.64 (0.22 . 4.60)	0.242
ARB-SV 14-day	23,770	****	****	****	****	4.59	****	-1.81	***	0.61 (0.22, 1.69)	0.342
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	22,933	****	****	****	****	4.64	****	0	****	1 00 / 0 25 2 95\	1
ARB-SV 14-day	22,933	****	****	****	****	4.64	****	U		1.00 (0.35, 2.85)	1
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	22,933	****	****	****	****	4.17	****	0.01	****	1.00 (0.35, 2.86)	0.994
ARB-SV 14-day	22,933	****	****	****	****	4.16	****	0.01		1.00 (0.55, 2.80)	0.554
					31	- 60 Days					
Site-Adjusted Analysi	s										
ACEI-SV 14-day	26,674	****	****	****	****	2.75	****	-2	****	0.57 (0.17, 1.87)	0.354
ARB-SV 14-day	18,475	****	****	****	****	4.76	****			0.57 (0.17, 1.07)	0.554
Fixed Ratio 1:1 Prope	nsity Score Mat	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	13,860	****	****	****	****	2.48	****	-2.48	****	0.50 (0.09, 2.73)	0.423
ARB-SV 14-day	13,860	****	****	****	****	4.97	****	-2.40		0.30 (0.03, 2.73)	0.423
Fixed Ratio 1:1 Prope	nsity Score Mat				•		<u> </u>	<u> </u>	<u> </u>		
ACEI-SV 14-day	17,726	****	****	****	****	1.66	****	-3.25	****	0.34 (0.07, 1.66)	0.181
ARB-SV 14-day	17,896	****	****	****	****	4.91	****	-3.23		0.54 (0.07, 1.00)	0.101

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						la dala a a		Incidence	D:#		
			A	A		Incidence		Rate	Difference		
		_	Average	Average		Rate per		Difference	in	Hazard Ratio	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per		Wald
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	18,122	****	****	****	****	2.98	****	-1.3	****	0.69 (0.17, 2.77)	0.601
ARB-SV 14-day	12,620	****	****	****	****	4.28	****				
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	6,482	****	****	****	****	2.3	****	-2.3	****	0.50 (0.05, 5.51)	0.571
ARB-SV 14-day	6,482	****	****	****	****	4.59	****	-2.5		0.30 (0.03, 3.31)	0.571
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco			iper= 0.05						
ACEI-SV 14-day	12,007	****	****	****	****	2.25	****	-2.16	****	0.51 (0.09, 2.77)	0.433
ARB-SV 14-day	12,247	****	****	****	****	4.41	****	-2.10		0.31 (0.03, 2.77)	0.433
					91 -	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	14,521	****	****	****	****	0.71	****	-2.38	****	0.23 (0.05, 1.16)	0.076
ARB-SV 14-day	10,137	****	****	****	****	3.09	****	-2.56		0.23 (0.05, 1.10)	0.076
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	4,171	****	****	****	****	0	****	4.74	****		
ARB-SV 14-day	4,171	****	****	****	****	4.74	****	-4.74	****	-	-
Fixed Ratio 1:1 Prope		tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	9,599	****	****	****	****	1.08	****	2.4	****	0.24 / 0.07 . 4.60\	0.407
ARB-SV 14-day	9,832	****	****	****	****	3.18	****	-2.1	ጥ ጥ ጥ ጥ	0.34 (0.07, 1.69)	0.187
,	·				181	- 270 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	9,359	****	****	****	****	2.07	****	0.55	****	1 27 / 0 25 7 40\	0.715
ARB-SV 14-day	6,444	****	****	****	****	1.52	****	0.55	4, 4, 4, 4,	1.37 (0.25, 7.49)	0.715

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Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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	Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	1,693	****	****	****	****	6.79	****	3.39	****	2.00 (0.18, 22.06)	0.571
ARB-SV 14-day	1,693	****	****	****	****	3.39	****	<u> </u>		2.00 (0.10, 22.00)	0.57 1
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	6,156	****	****	****	****	3.17	****	1.61	****	2.01 / 0.27 .10.07\	0.421
ARB-SV 14-day	6,269	****	****	****	****	1.56	****	1.61		2.01 (0.37, 10.97)	0.421
					271	- 365 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day	6,661	****	****	****	****	1.35	****	0.22	****	4.25 / 0.42 .44.00\	0.000
ARB-SV 14-day	4,510	****	****	****	****	1.02	****	0.33	the she she she she	1.35 (0.12, 14.90)	0.806
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	870	****	****	****	****	0	****	0	****		
ARB-SV 14-day	870	****	****	****	****	0	****	0	the she she she she	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	4,321	****	****	****	****	0	****	1.04	****		
ARB-SV 14-day	4,396	****	****	****	****	1.04	****	-1.04	ren ren ren ren	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

Companies	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) ¹	Wald P-Value ¹
ACEI-SV 14-day 48,892 ***** **** **** * 2.44 ***** 1.1 ***** 1.86 (1.09, 3.15) 0.022 ACEI-SV 14-day 38,268 *** **** **** **** * 2.56 (1.18, 5.52) 0.017 ACEI-SV 14-day 38,268 *** **** *** **** * 2.56 (1.18, 5.52) 0.017 ACEI-SV 14-day 38,268 *** *** *** **** * 2.56 (1.18, 5.52) 0.017 ACEI-SV 14-day 38,268 *** *** *** * 2.56 **** * 2.56 **** * 2.56 (1.18, 5.52) 0.017 ACEI-SV 14-day 38,268 *** *** *** * 2.56 **** * 1.26 ***** * 1.98 (1.11, 3.53) 0.02 Site-Adjusted Analysis							Overall					
Section 19-10 Section 19-1												
Sive Action 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.062	•	•							1.1	****	1.86 (1.09. 3.15)	0.022
ACEI-SV 14-day 38,268 ******							1.34	****				
Size		ensity Score Ma										
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 ***** ***** ***** ***** 1.3 ***** 1.26 ****** 1.98 (1.11, 3.53) 0.02 Site-Adjusted Analysis ACEI-SV 14-day 48,892 ***** ***** ***** ***** 1.15 ***** 2.8 ***** 3.40 (1.12, 10.34) 0.031 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 ***** ***** ***** ***** 4.83 ****** 3.34 ***** 3.25 (1.06, 9.97) 0.039 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 ***** ***** ***** ***** 4.68 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 ***** ***** ***** ***** 4.68 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** ***** ***** ***** 1.31 ***** 3.37 ***** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 37,272 ***** ***** ***** ***** 1.49 ***** 2.47 ***** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 26,730 ***** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 26,730 ***** ***** ***** ***** 1.97 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** ***** 4.59 ****** 2.62 ****** 2.33 (0.60, 9.02) 0.22	ACEI-SV 14-day	38,268					3.4		2.07	****	2 56 (1 18 5 52)	0.017
ACEI-SV 14-day 38,268 ***** **** **** **** 1.3 ***** 1.26 ***** 1.98 (1.11, 3.53) 0.02 Site-Adjusted Analysis							1.33	****			2.30 (1.10, 3.32)	
Sy												
Site-Adjusted Analysis ACEI-SV 14-day 48,892 ***** ***** ***** ***** 1.15 ***** 2.8 ***** 3.40 (1.12, 10.34) 0.031 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 ***** ***** ***** 4.83 ***** 3.34 ***** 3.25 (1.06, 9.97) 0.039 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 ***** ***** ***** 4.68 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 **** **** ***** ***** 1.31 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** ***** ***** ***** 1.49 ***** 2.47 ***** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 26,730 ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** 4.07 ***** 2.8 ***** 3.16 (0.84 11.93) 0.089	•	•							1.26	****	1.98 (1.11, 3.53)	0.02
ACEI-SV 14-day	SV	38,268	****	****	****			****				
ACEI-SV 14-day 48,892 ***** ***** ***** ***** ***** ***** 1.15 ***** 2.8 ***** 3.40 (1.12, 10.34) 0.031 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 **** ***** ***** ***** 4.83 ***** 3.34 ***** 3.25 (1.06, 9.97) 0.039 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 **** **** ***** ***** 4.68 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 ACEI-SV 14-day 38,268 **** **** ***** ***** ***** 1.31 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** ***** ***** ***** ***** 1.49 ***** 2.47 ***** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 26,730 ***** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** 4.07 ***** 2.8 ***** 3.16 (0.84 11.93) 0.089						0	- 30 Days					
Size			44444	*****	****	*****		4. 4. 4. 4. 4.				
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ² ACEI-SV 14-day 38,268 **** **** ***** 1.49 ***** 3.34 ***** 3.25 (1.06, 9.97) 0.039 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 **** **** ***** ***** 1.31 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** **** ***** ***** 3.96 ***** 2.47 ***** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ² ACEI-SV 14-day 26,730 **** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ² ACEI-SV 14-day 26,730 **** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** 4.07 ***** 4.07 ****** 3.16 (0.84 11.93) 0.089	•	•							2.8	****	3.40 (1.12, 10.34)	0.031
ACEI-SV 14-day 38,268 ***** **** **** **** **** 4.83 ***** 3.34 ***** 3.25 (1.06, 9.97) 0.039 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 **** **** **** **** 4.68 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** **** **** **** 3.96 ***** 2.47 ***** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 14-day 26,730 **** **** **** **** 4.59 **** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** **** **** **** 4.59 **** 2.62 ***** 3.36 (0.60, 9.02) 0.22							1.15	4, 4, 4, 4, 4,			· · ·	
SV 38,268 **** **** **** **** **** **** * 1.49 ***** 3.34 ***** 3.25 (1.06, 9.97) 0.039 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05								de de de de				
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 38,268 ***** ***** ***** ***** 4.68 ***** 3.37 ***** 3.55 (1.16, 10.89) 0.027 Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** ***** ***** ***** 3.96 ***** 2.47 ***** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 14-day 26,730 ***** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** 4.07 ***** 2.8 ***** 3.16 (0.84, 11.93) 0.089	•	,							3.34	****	3.25 (1.06, 9.97)	0.039
ACEI-SV 14-day 38,268 **** **** **** **** **** 4.68 **** 3.37 **** 3.55 (1.16, 10.89) 0.027 Site-Adjusted Analysis							1.49	****				
Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** **** **** **** **** **** ***						•	1.50	4. 4. 4. 4. 4.				
Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** **** **** **** **** 1.49 ***** 2.47 **** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 26,730 **** **** **** **** 4.59 **** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 **** **** **** **** 4.07 ***** 2.82 ***** 3.16 (0.84, 11.93) 0.089	-	•							3.37	****	3.55 (1.16, 10.89)	0.027
Site-Adjusted Analysis ACEI-SV 14-day 37,272 ***** ***** ***** 3.96 ***** ***** 2.47 ****** 2.65 (0.83, 8.46) 0.099 Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 14-day 26,730 ***** ***** ***** ***** 4.59 ***** ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ****** ****** ****** 4.07 ****** 3 16 (0.84 11 93) 0.089	SV	38,268	****	****	****			*****				
ACEI-SV 14-day 37,272 ***** **** **** **** **** 3.96 ***** 2.47 **** 2.65 (0.83, 8.46) 0.099 SV 40,092 **** **** **** **** **** 4.59 **** 2.62 **** 2.33 (0.60, 9.02) Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 26,730 **** **** **** **** **** 1.97 ***** 2.62 **** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 **** **** **** ****	Site Adjusted Analys	ic				31	- 60 Days					
SV 40,092 ***** **** **** **** **** ****			****	****	****	****	2 06	****				
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ² ACEI-SV 14-day 26,730 ***** ***** ***** ***** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 SV 26,730 ***** **** ***** ***** ***** ***** 1.97 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** 4.07 ***** 2.8 ***** 3.16 (0.84.11.93) 0.089	•	•							2.47	****	2.65 (0.83, 8.46)	0.099
ACEI-SV 14-day 26,730 ***** **** **** **** 4.59 ***** 2.62 ***** 2.33 (0.60, 9.02) 0.22 SV 26,730 **** **** **** **** **** **** **** 1.97 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 **** **** **** ACEI-SV 14-day 29,086 ***** ACEI-SV 14-day 29,086 ***** ACEI-SV 14-day 29,086 ***** ACEI-S				litianal Ana			1.45					
SV 26,730 ***** **** **** **** **** 2.33 (0.60, 9.02) 0.22 Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** **** **** **** **** 4.07 ***** 2.8 ***** 3.16 (0.84, 11.93) 0.089							4 E0	****				
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 29,086 ***** ***** ***** ***** 4.07 ***** 2.8 ***** 3.16 (0.84.11.93) 0.089	•	•							2.62	****	2.33 (0.60, 9.02)	0.22
ACEI-SV 14-day 29,086 ***** ***** ***** 4.07 ***** 2.8 ***** 3.16 (0.84, 11.93) 0.089							1.97					
ACLI-3V 14-day 25,080 4.07 2.8 ***** 3.16 (0.84 11.93) 0.089	-	•				•	4.07	****				
\\\ \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	SV	35,104	****	****	****	****	1.27	****	2.8	****	3.16 (0.84, 11.93)	0.089

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

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) ¹	Wald P-Value ¹
					61	- 90 Days				,	
Site-Adjusted Analys	sis										
ACEI-SV 14-day	25,060	****	****	****	****	2.7	****	0.67	****	1.32 (0.35, 4.91)	0.681
SV	26,220	****	****	****	****	2.03	****	0.07		1.32 (0.33, 4.31)	0.001
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	11,751	****	****	****	****	0	****	-1.26	****		_
SV	11,751	****	****	****	****	1.26	****	-1.20			
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	19,427	****	****	****	****	1.4	****	-0.33	****	0.80 (0.13, 4.79)	0.807
SV	23,009	****	****	****	****	1.73	****			0.00 (0.13, 4.73)	——————————————————————————————————————
					91	- 180 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	19,855	****	****	****	****	0.78	****	-0.82	****	0.49 (0.12, 1.98)	0.319
SV	21,275	****	****	****	****	1.6	****			(- , ,	
Fixed Ratio 1:1 Prop											
ACEI-SV 14-day	7,579	****	****	****	****	1.85	****	1.85	****	_	_
SV	7,579	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	•										
ACEI-SV 14-day	15,292	****	****	****	****	1.02	****	-0.48	****	0.70 (0.17, 2.93)	0.622
SV	18,774	****	****	****	****	1.5	****			(- , ,	
Cita Adinatad Amelia					181	- 270 Days					
Site-Adjusted Analys		****	****	****	****	1 01	****				
ACEI-SV 14-day	12,717	****	****	****	****	1.91	****	1.01	****	2.06 (0.40, 10.63)	0.387
SV	11,517					0.9	100 100 100 100 100				
Fixed Ratio 1:1 Prop		tched Cond	itional Ana	lysis; Calipe	*****		****				
ACEI-SV 14-day	2,696	****	****	****	****	0	****	0	****	-	-
SV	2,696					0	****				
Fixed Ratio 1:1 Prop	•	tched Unco	*****	nalysis; Cali	*****	1 52	****				
ACEI-SV 14-day	9,596	****	****	****	****	1.53	****	0.54	****	1.50 (0.25, 8.99)	0.656
SV	10,345	~~~~~	7-7-4-4	70 TO TO TO TO	~~~~~	0.99	77 77 77 7			·	

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

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) ¹	Wald P-Value ¹
					271	- 365 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	9,003	****	****	****	****	1.5	****	0.05	****	2 20 / 0 24 22 11\	0.472
SV	7,202	****	****	****	****	0.65	****	0.85		2.30 (0.24, 22.11)	0.472
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	1,234	****	****	****	****	4.49	****	0	****	1.00 / 0.00 15.00\	1
SV	1,234	****	****	****	****	4.49	****	0	4.4.4.4.4.	1.00 (0.06, 15.99)	1
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	6,637	****	****	****	****	2.07	****	1 26	****	2.00 / 0.20 27.76\	0.350
SV	6,565	****	****	****	****	0.71	****	1.36		2.89 (0.30, 27.76)	0.359

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

Medical Product No Angioedema (-183,	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) ¹	Wald P-Value ¹
No Anglocaema (103)	-,					Overall					
Site-Adjusted Analysis											
ACEI-SV 14-day SV	48,846 43,990	****	****	*****	*****	2.38 1.09	****	1.29	****	2.23 (1.26, 3.94)	0.006
Fixed Ratio 1:1 Propen	sity Score Mat	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day SV	38,210 38,210	****	****	*****	****	3.26 0.89	****	2.37	****	3.67 (1.49, 9.04)	0.005
Fixed Ratio 1:1 Propen	sity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV 14-day	38,210	****	****	****	****	2.48	*****	1.47	****	2.46 (1.31, 4.63)	0.005
SV	38,210	44444	4.4.4.4.	4-4-4-4-4-		1.01 - 30 Days	4.4.4.4.4				
Site-Adjusted Analysis					<u> </u>	- 30 Days					
ACEI-SV 14-day	48,846	****	****	****	****	3.95	****				
SV	43,990	****	****	****	****	0.57	****	3.37	****	6.79 (1.54, 29.86)	0.011
Fixed Ratio 1:1 Propen	sity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	38,210	****	****	****	****	4.83	****	4.09	****	6.50 (1.47, 28.80)	0.014
SV	38,210	****	****	****	****	0.74	****	4.03		0.30 (1.47, 20.00)	0.014
Fixed Ratio 1:1 Propen											
ACEI-SV 14-day	38,210	****	****	****	****	4.69	****	4.03	****	7.08 (1.60, 31.39)	0.01
SV	38,210	****	****	****	****	0.66	****			(,,	
Site-Adjusted Analysis					31	- 60 Days					
ACEI-SV 14-day	37,236	****	****	****	****	3.57	****				
SV	40,039	****	****	****	****	1.49	****	2.08	****	2.38 (0.73, 7.74)	0.148

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Table 15. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²					•	
ACEI-SV 14-day	26,690	****	****	****	****	3.94	****	4.07	****	2.00 (0.50 0.00)	0.227
SV	26,690	****	****	****	****	1.97	****	1.97	****	2.00 (0.50, 8.00)	0.327
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	29,046	****	****	****	****	3.57	****	2.20	****	2.76 / 0.71 10.67	0.141
SV	35,052	****	****	****	****	1.27	****	2.29		2.76 (0.71, 10.67)	0.141
					61	- 90 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	25,039	****	****	****	****	2.7	****	1.18	****	1.76 (0.42, 7.35)	0.44
SV	26,182	****	****	****	****	1.53	****	1.10		1.70 (0.42, 7.55)	0.44
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	11,731	****	****	****	****	0	****	0	****		
SV	11,731	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	19,402	****	****	****	****	1.4	****	0.24	****	1.20 (0.17, 8.52)	0.855
SV	22,969	****	****	****	****	1.16	****	0.24		1.20 (0.17, 6.32)	0.833
					91	- 180 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	19,842	****	****	****	****	0.78	****	-0.56	****	0.60 (0.14, 2.51)	0.481
SV	21,244	****	****	****	****	1.34	****	-0.50		0.00 (0.14, 2.31)	0.401
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	7,574	****	****	****	****	1.85	****	1.85	****		
SV	7,574	****	****	****	****	0	****	1.85		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	15,278	****	****	****	****	1.03	****	-0.18	****	0.88 (0.20, 3.95)	0.868
SV	18,743	****	****	****	****	1.21	****	-0.10		0.00 (0.20, 3.93)	0.000

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Table 15. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

	Number of	Person Years	Average Person Days	Average Person Years	Number of	Incidence Rate per 1,000 Person	Risk per 1,000	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	_	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
iviedicai Product	New Users	at KISK	at RISK	at RISK	Events 181	- 270 Days	New Osers	rears	New Osers	intervalj	P-value
Site-Adjusted Analysi	c				101	- 270 Days					
ACEI-SV 14-day	12,707	****	****	****	****	1.91	****				
SV	11,500	****	****	****	****	0.9	****	1.01	****	2.06 (0.40, 10.62)	0.388
		habad Cana	ditional Ana	lucia. Calina	0 0F ²	0.5					
Fixed Ratio 1:1 Prope		*****	*****	****	*****	0	****				
ACEI-SV 14-day SV	2,698 2,698	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prope						U					
•	9,587	****	*****	*****	*****	1.54	****				
ACEI-SV 14-day SV	9,587 10,330	****	****	****	****	1.54	****	0.54	****	1.50 (0.25, 8.98)	0.657
3 V	10,550					- 365 Days					
Site-Adjusted Analysi	c				2/1	- 303 Days					
ACEI-SV 14-day	8,995	****	****	****	****	1.5	****				
SV	7,191	****	****	****	****	0.66	****	0.85	****	2.29 (0.24, 22.09)	0.473
		habad Cana	ditional Ana	lucia. Calina	0 0F ²	0.00					
Fixed Ratio 1:1 Prope		*****	*****	****	*****	4.48	****				
ACEI-SV 14-day SV	1,234 1.234	****	****	****	****	4.48 4.48	****	0	****	1.00 (0.06, 15.99)	1
Fixed Ratio 1:1 Prope	, -					4.48					
ACEI-SV 14-day	6,631	****	*****	*****	*****	2.07	****				
•	•	****	****	****	****		****	1.36	****	2.88 (0.30, 27.73)	0.359
SV Angioedema (-183, -1	6,557					0.71					
Angioedema (-183, -1	-)					Overall					
Site-Adjusted Analysi	e					Overall					
Site-Aujusteu Allaiysi	3										
ACEI-SV 14-day	46	****	****	****	****	77.34	****				

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Table 15. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prop							030.3		TICH COCIO	e.rui,	
ACEI-SV 14-day	30	****	****	****	****	239.23	****				
SV	30	****	****	****	****	478.47	****	-239.23	****	0.50 (0.05, 5.51)	0.571
Fixed Ratio 1:1 Prop		tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	30	****	****	****	****	138.12	****	474.24	****	0.44/0.05 4.44	0.47
SV	30	****	****	****	****	309.36	****	-171.24	****	0.44 (0.05, 4.14)	0.47
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	46	****	****	****	****	0	****	-421.94	****	_	_
SV	60	****	****	****	****	421.94	****	-421.94			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	30	****	****	****	****	0	****	-952.38	****		
SV	30	****	****	****	****	952.38	****	-952.38		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	30	****	****	****	****	0	****	-854.7	****		
SV	30	****	****	****	****	854.7	****	-634.7			
					31	- 60 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	39	****	****	****	****	371.75	****	371.75	****	_	_
SV	55	****	****	****	****	0	****	371.73			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	21	****	****	****	****	645.16	****	645.16	****		
SV	21	****	****	****	****	0	****	043.10		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cal	•						
ACEI-SV 14-day	24	****	****	****	****	574.71	****	574.71	****	_	
SV	26	****	****	****	****	0	****	3/4./1		-	_

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Table 15. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	25	****	****	****	****	0	****	-336.7	****	_	_
SV	40	****	****	****	****	336.7	****	-330.7			
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	18	****	****	****	****	0	****	0	****		
SV	18	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	20	****	****	****	****	0	****	-564.97	****		
SV	26	****	****	****	****	564.97	****	-304.97		-	-
					91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	17	****	****	****	****	0	****	-157.48	****		
SV	32	****	****	****	****	157.48	****	-137.46		-	-
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	11	****	****	****	****	0	****	-260.42	****		
SV	19	****	****	****	****	260.42	****	-200.42		-	-
					181	- 270 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	11	****	****	****	****	0	****	0	****		
SV	21	****	****	****	****	0	****	U		-	-

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Table 15. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

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) ¹	Wald P-Value ¹
Fixed Ratio 1:1 Prope							THE TOTAL TO		TICH COCIO		
ACEI-SV 14-day SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day SV	****	****	****	*****	*****	0 0	****	0	****	-	-
					271	- 365 Days					
Site-Adjusted Analysi	is										
ACEI-SV 14-day SV	****	*****	****	*****	****	0 0	****	0	****	-	-
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		<u>-</u>	<u>-</u>
Fixed Ratio 1:1 Prope	nsity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day SV	****	****	*****	****	*****	0 0	****	0	****	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Unknown											
						Overall					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	7,919	****	****	****	****	1.58	****	0.83	****	2.18 (0.40, 11.95)	0.369
SV	7,229	****	****	****	****	0.75	****	0.83		2.18 (0.40, 11.93)	0.309
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	5,986	****	****	****	****	0.99	****	0.99	****		
SV	5,986	****	****	****	****	0	****	0.99		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	5,986	****	****	****	****	1.6	****	0.72	****	1.92 (0.32, 11.58)	0.475
SV	5,986	****	****	****	****	0.88	****	0.72		1.52 (0.52, 11.56)	0.473
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	7,919	****	****	****	****	1.79	****	1.79	****	_	_
SV	7,229	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	5,986	****	****	****	****	0	****	0	****	_	_
SV	5,986	****	****	****	****	0	****	0		_	
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV 14-day	5,986	****	****	****	****	0	****	0	****	_	_
SV	5,986	****	****	****	****	0	****			_	
					31	- 60 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	5,644	****	****	****	****	2.59	****	2.59	****	_	_
SV	6,518	****	****	****	****	0	****	2.55			

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

Medical Product New Users at Risk at R									Incidence			
Number of Person Person Person Person Days Vears Of Person 1,000 Pers							Incidence		Rate	Difference		
Number of Years Days Years of Person 1,000 Person 1,000 (95% Confidence Number of Years At Risk at Risk at Risk Events Years New Users Years New Users New Users Interval) Person 1,000 (95% Confidence Number of Years New Users				Average	Average		Rate per		Difference	in		
Medical Product New Users at Risk at Risk at Risk at Risk at Risk st Risk at Risk st Risk at Risk st R			Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per		
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ² ACEI-SV 14-day 3,901 ***** ***** ***** ***** 4.45 ***** 4.45 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ACEI-SV 14-day 4,250 **** **** ***** ***** 0.***** 3.45 ***** ACEI-SV 14-day 3,863 ***** ***** ***** ***** 3.53 ***** ACEI-SV 14-day 3,863 ***** **** ***** ***** 3.53 ***** ACEI-SV 14-day 3,863 ***** **** ***** ***** 3.04 ***** 0.48 ***** 1.09 (0.07, 17.44) (0.07, 1		Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
ACEI-SV 14-day 3,901 ***** ***** ***** ***** 4,45 ***** 4,45 ***** 4,45 ***** - SV 3,901 ***** ***** ***** ***** ***** 0 ****** 4,45 ***** 4,45 ***** - SV 3,901 ***** ***** ***** ***** 0 ***** 4,45 ***** 4,45 ***** - SV 5,457 ***** ***** ***** ***** 0 ***** 3,45 ***** 3,45 ***** ****	Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Sy	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day	ACEI-SV 14-day	3,901	****	****	****	****	4.45	****	1 1E	****		
ACEI-SV 14-day	SV	3,901	****	****	****	****	0	****	4.45		-	-
Site-Adjusted Analysis	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
Site-Adjusted Analysis	ACEI-SV 14-day	4,250	****	****	****	****	3.45	****	2 //5	****	_	_
ACEI-SV 14-day 3,863 ***** ***** ***** ***** ***** 3.53 ***** ***** 3.04	SV	5,457	****	****	****	****	0	****	5.45		-	
ACEI-SV 14-day 3,863 ***** **** ***** ***** 3.53 ***** 0.48 ***** 1.09 (0.07, 17.44) (Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 14-day 1,763 ***** ***** ***** ***** 0 ****** 0 ******						61	- 90 Days					
Size	Site-Adjusted Analys	sis										
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05² ACEI-SV 14-day 1,763 ***** ***** ***** 0 ****** 0 ****** 0 ******	ACEI-SV 14-day	3,863			****	****	3.53		0.48	****	1 09 (0 07 17 44)	0.951
ACEI-SV 14-day 1,763 ***** **** **** ***** 0 ***** 0 ***** 0 ***** 5 V 1,763 ***** **** **** **** **** **** 0 ***** 0 ***** 1,763 ***** **** **** **** 0 ***** 0 ***** 1,763 ***** ****		,					3.04	****	0.46		1.09 (0.07, 17.44)	0.931
ACEI-SV 14-day 1,763 ***** **** ***** ***** 0 ***** 0 ***** 0 ***** 5 V 1,763 ***** **** **** **** **** **** 0 ***** 0 *****	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
SV			****	****			0	****	0	****		
ACEI-SV 14-day 2,894 ***** **** **** **** **** 4.74 ***** 1.14 ***** 1.29 (0.08, 20.62) (0.08, 20.62	SV	1,763	****	****	****	****	0	****	U		-	-
Site-Adjusted Analysis ACEI-SV 14-day	Fixed Ratio 1:1 Prop	ensity Score Mat	tched Unco	onditional A	nalysis; Cali	per= 0.05						
Site-Adjusted Analysis ACEI-SV 14-day 3,024 ***** ***** ***** **** ***** 1.55 ***** -1.55 ***** - Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 1,104 ***** **** ***** 0 ***** 0 ***** 0 ***** - SV 1,104 ***** ***** ***** 0 ****** 0 ****** 0 ******	ACEI-SV 14-day	2,894	****	****	****	****	4.74	****	1 1/1	****	1 20 / 0 09 20 62)	0.858
Site-Adjusted Analysis ACEI-SV 14-day 3,024 ***** ***** ***** 0 ****** -1.55 ***** - SV 3,550 ***** ***** ***** 1.55 ***** -	SV	3,703	****	****	****	****	3.6	****	1.14		1.29 (0.08, 20.62)	0.656
ACEI-SV 14-day 3,024 **** **** **** **** **** 0 ***** -1.55 **** -1.55 **** - SV 3,550 **** **** **** **** 1.55 ***** -1.55 ***** - Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ***** 0 ***** 0 ***** ACEI-SV 14-day 1,104 **** **** **** **** 0 ***** 0 ***** SV 1,104 **** **** **** **** 0 ***** 0 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05						91	- 180 Days					
SV 3,550 **** **** **** **** **** 1.55 ***** -1.55 **** -1.55 **** -1.55 ***** -1.55 ***** -1.55 ***** -1.55 *****	Site-Adjusted Analys											
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ACEI-SV 14-day 1,104 ***** ***** ***** 0 ****** SV 1,104 ***** ***** ***** 0 ****** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05	ACEI-SV 14-day	3,024					0		-1 55	****	_	_
ACEI-SV 14-day 1,104 ***** **** ***** 0 ***** 0 ***** 5V 1,104 ***** **** **** **** 0 ***** 0 ***** - Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05							1.55	****	1.55			
ACEI-SV 14-day 1,104 ***** **** ***** 0 ***** 0 ***** 5V 1,104 ***** **** **** **** 0 ***** 0 ***** - Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
SV 1,104 **** **** **** 0 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05			****	****			0	****	0	****		
	SV	1,104	****	****	****	****	0	****			<u> </u>	<u>-</u>
ACTICV/4/4 Jan. 2 225 ***** ***** ***** A**** O *****	Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-5V 14-day 2,235 -1.8 ***** -	ACEI-SV 14-day	2,235	****	****	****	****	0	****	_1 0	****		
SV 3,011 **** **** **** 1.8 ****	SV	3,011	****	****	****	****	1.8	****	-1.0		-	-

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1.000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					181	- 270 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day	1,953	****	****	****	****	0	****	0	****		
SV	2,030	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	400	****	****	****	****	0	****	0	****		
SV	400	****	****	****	****	0	****	0	the de de de de	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	1,427	****	****	****	****	0	****	0	****		
SV	1,773	****	****	****	****	0	****	0		-	
					271	- 365 Days					
Site-Adjusted Analys	is										
ACEI-SV 14-day	1,379	****	****	****	****	3.25	****	3.25	****	_	_
SV	1,283	****	****	****	****	0	****	3.23			
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	180	****	****	****	****	0	****	0	****	_	_
SV	180	****	****	****	****	0	****				
Fixed Ratio 1:1 Prope	ensity Score Ma				•						
ACEI-SV 14-day	996	****	****	****	****	4.54	****	4.54	****	_	_
SV	1,140	****	****	****	****	0	****	4.54			
Race: American India	an										
						Overall					
Site-Adjusted Analys		at at at at at	distribute de d	4.4.4.4	4.4.4.4						
ACEI-SV 14-day	160	****	****	****	****	0	****	0	****	-	_
SV	143	****	****	****	****	0	****	-			

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	98	****	****	****	****	0	****	0	****		
SV	98	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	98	****	****	****	****	0	****	0	****	_	_
SV	98	****	****	****	****	0	****	0			
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	160	****	****	****	****	0	****	0	****	_	_
SV	143	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	98	****	****	****	****	0	****	0	****	_	_
SV	98	****	****	****	****	0	****	0			
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	98	****	****	****	****	0	****	0	****	_	_
SV	98	****	****	****	****	0	****				
					31	- 60 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	120	****	****	****	****	0	****	0	****	_	_
SV	125	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	60	****	****	****	****	0	****	0	****	_	_
SV	60	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	71	****	****	****	****	0	****	0	****	_	_
SV	84	****	****	****	****	0	****	J			

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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) ¹	Wald P-Value ¹
					61	- 90 Days					
Site-Adjusted Analy											
ACEI-SV 14-day	77	****	****	****	****	0	****	0	****	_	_
SV	85	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	25	****	****	****	****	0	****	0	****		
SV	25	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	43	****	****	****	****	0	****	0	****	_	_
SV	56	****	****	****	****	0	****	0			
					91	- 180 Days					
Site-Adjusted Analy											
ACEI-SV 14-day	61	****	****	****	****	0	****	0	****	_	_
SV	64	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	18	****	****	****	****	0	****	0	****		
SV	18	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	37	****	****	****	****	0	****	0	****	_	_
SV	46	****	****	****	****	0	****				
					181	- 270 Days					
Site-Adjusted Analy											
ACEI-SV 14-day	37	****	****	****	****	0	****	0	****	_	_
SV	33	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop											
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****			<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	23	****	****	****	****	0	****	0	****	_	_
SV	26	****	****	****	****	0	****	J		_	-

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					271	- 365 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	28	****	****	****	****	0	****	0	****		
SV	19	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	***	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	17	****	****	****	****	0	****	0	****		
SV	15	****	****	****	****	0	****	U		-	
Race: Asian											
						Overall					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	525	****	****	****	****	0	****	0	****	_	_
SV	537	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	414	****	****	****	****	0	****	0	****		
SV	414	****	****	****	****	0	****	<u> </u>		<u> </u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05		_	_	_	_	
ACEI-SV 14-day	414	****	****	****	****	0	****	0	****		
SV	414	****	****	****	****	0	****	J		-	-

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	525	****	****	****	****	0	****	0	****		
SV	537	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	414	****	****	****	****	0	****		****		
SV	414	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	414	****	****	****	****	0	****	0	****		
SV	414	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	381	****	****	****	****	0	****	0	****		
SV	496	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	281	****	****	****	****	0	****		****		
SV	281	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	304	****	****	****	****	0	****		****		
SV	384	****	****	****	****	0	****	0	****	-	-
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	260	****	****	****	****	0	****	0	****		
SV	337	****	****	****	****	0	****	0	nen nen nen nen nen	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	126	****	****	****	****	0	****	-	****		
SV	126	****	****	****	****	0	****	0	ጥ ጥ ጥ ጥ	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	201	****	****	****	****	0	****	0	****		
SV	260	****	****	****	****	0	****	0		-	-

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Wieuicai Fiouuct	New Osers	at Misk	αι Νίοκ	at Misk		- 180 Days	New Osers	ieais	INEW OSEIS	iiiteivaij	r-value
Site-Adjusted Analys	sis					100 Days					
ACEI-SV 14-day	195	****	****	****	****	0	****	_	de de de de		
SV	258	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	litional Ana	lysis: Calipe	r= 0.05 ²						
ACEI-SV 14-day	71	****	****	****	****	0	****	_	****		
SV	71	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Propo	ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	152	****	****	****	****	0	****	0	****		
SV	204	****	****	****	****	0	****	0		-	-
					181	270 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	134	****	****	****	****	0	****	0	****	_	_
SV	139	****	****	****	****	0	****				
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	22	****	****	****	****	0	****	0	****		
SV	22	****	****	****	****	0	****			<u>-</u>	
Fixed Ratio 1:1 Prope					•						
ACEI-SV 14-day	104	****	****	****	****	0	****	0	****	-	_
SV	105	****	****	****	*****	0	****				
					271	365 Days					
Site-Adjusted Analys		****	****	****	****		****				
ACEI-SV 14-day	101	****	****	****	****	0	****	0	****	-	_
SV	89					0	****				
Fixed Ratio 1:1 Propo							de de de de				
ACEI-SV 14-day	15	****	****	****	****	0	****	0	****	-	-
SV	15					0	****				
Fixed Ratio 1:1 Propo		tched Unco	nditional A	nalysis; Cal	*****		****				
ACEI-SV 14-day	76	****	****	****	****	0	****	0	****	-	-
SV Race: Black	71	*****	****	****	****	0	****				

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
						Overall					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	5,969	****	****	****	****	6.92	****	2.95	****	1.79 (0.70, 4.55)	0.223
SV	5,968	****	****	****	****	3.96	****	2.93		1.79 (0.70, 4.33)	0.223
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	4,916	****	****	****	****	10.79	****	C 74	****	2.67/0.71 10.05\	0.147
SV	4,916	****	****	****	****	4.05	****	6.74		2.67 (0.71, 10.05)	0.147
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	4,916	****	****	****	****	7.05	****	3.01	****	1.80 (0.65, 4.96)	0.256
SV	4,916	****	****	****	****	4.04	****	5.01		1.80 (0.65, 4.96)	0.236
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	5,969	****	****	****	****	13.97	****	11.85	****	6.43 (0.77, 53.41)	0.085
SV	5,968	****	****	****	****	2.12	****	11.05		0.43 (0.77, 33.41)	0.005
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	4,916	****	****	****	****	17.46	****	14.55	****	6.00 / 0.72 / 0.94\	0.007
SV	4,916	****	****	****	****	2.91	****	14.55		6.00 (0.72, 49.84)	0.097
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	4,916	****	****	****	****	16.92	****	14.36	****	6.51 (0.78, 54.09)	0.083
SV	4,916	****	****	****	****	2.56	****	14.50		0.51 (0.76, 54.09)	0.065
					31	60 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	4,445	****	****	****	****	13.8	****	10.9	****	4.85 (0.54, 43.40)	0.158
SV	5,422	****	****	****	****	2.9	****	10.5		4.03 (0.54, 45.40)	0.130
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	3,379	****	****	****	****	11.15	****	11.15	****		
SV	3,379	****	****	****	****	0	****	11.13			
Fixed Ratio 1:1 Prop	.				•						
ACEI-SV 14-day	3,684	****	****	****	****	12.49	****	9	****	3.69 (0.38, 35.49)	0.259
SV	4,519	****	****	****	****	3.49	****	Э		J.UJ (U.JO, JJ.43)	0.233

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	2,740	****	****	****	****	0	****	-4.38	****	_	_
SV	3,115	****	****	****	****	4.38	****	4.50			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	1,211	****	****	****	****	0	****	-12.61	****		
SV	1,211	****	****	****	****	12.61	****	-12.01		-	
Fixed Ratio 1:1 Prop					•						
ACEI-SV 14-day	2,271	****	****	****	****	0	****	-5.28	****	_	_
SV	2,577	****	****	****	****	5.28	****	3.20			
					91	- 180 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	2,051	****	****	****	****	2.61	****	-2.67	****	0.47 (0.04, 5.21)	0.54
SV	2,364	****	****	****	****	5.28	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond		lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	691	****	****	****	****	0	****	-11.22	****	_	_
SV	691	****	****	****	****	11.22	****	-11.22			
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	1,690	****	****	****	****	3.21	****	0.07	****	0.97 (0.06, 15.56)	0.985
SV	1,968	****	****	****	****	3.13	****	0.07		0.57 (0.00, 15.50)	0.565
					181	- 270 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	1,228	****	****	****	****	3.99	****	-5.87	****	0.40 (0.04, 4.42)	0.456
SV	1,074	****	****	****	****	9.86	****				
Fixed Ratio 1:1 Prop	ensity Score Ma										
ACEI-SV 14-day	198	****	****	****	****	0	****	0	****		
SV	198	****	****	****	****	0	****	<u> </u>			
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ACEI-SV 14-day	995	****	****	****	****	0	****	-11.28	****	_	_
SV	927	****	****	****	****	11.28	****	11.20			

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					271	- 365 Days					
Site-Adjusted Analy	sis										
ACEI-SV 14-day	838	****	****	****	****	0	****	0	****		
SV	661	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	98	****	****	****	****	0	****	0	****		
SV	98	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	677	****	****	****	****	0	****	0	****		
SV	587	****	****	****	****	0	****	0	To the steel steel	-	-

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Pacific Islande	r										
						Overall					
Site-Adjusted Analys											
ACEI-SV 14-day	46	****	****	****	****	0	****	0	****	_	_
SV	47	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	38	****	****	****	****	0	****	0	****		
SV	38	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	38	****	****	****	****	0	****	0	****		
SV	38	****	****	****	****	0	****	0		_	_
					0	- 30 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	46	****	****	****	****	0	****	0	****		
SV	47	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Con	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	38	****	****	****	****	0	****	0	****		
SV	38	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	38	****	****	****	****	0	****	0	****		
SV	38	****	****	****	****	0	****			<u>-</u>	
					31	- 60 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	33	****	****	****	****	0	****	0	****	_	
SV	43	****	****	****	****	0	****	U		-	-

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	25	****	****	****	****	0	****	0	****		
SV	25	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	27	****	****	****	****	0	****	0	****		
SV	35	****	****	****	****	0	****	0		-	-
					61	- 90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	22	****	****	****	****	0	****	0	****		
SV	28	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	18	****	****	****	****	0	****	0	****		
SV	23	****	****	****	****	0	****	U		-	-
					91	- 180 Days					
Site-Adjusted Analys											
ACEI-SV 14-day	19	****	****	****	****	0	****	0	****		
SV	26	****	****	****	****	0	****			<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ACEI-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	nan nan nan nan	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	15	****	****	****	****	0	****	0	****		
SV	21	****	****	****	****	0	****	U		-	-

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

							Incidence			
	_	•	•						Harand Datio	
					•	•	• •	-		
Number of		Days		of	Person	1,000	Person	•	•	Wald
New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
				181	- 270 Days					
					0		Ο	****	_	_
15	****	****	****	****	0	****				
nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
****	****	****	****	****	0	****	0	****		
****	****	****	****	****	0	****	U	4.4.4.4.4.	-	-
nsity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
11	****	****	****	****	0	****		****		
12	****	****	****	****	0	****	U	4.4.4.4.4.	-	-
				271	- 365 Days					
s										
****	****	****	****	****	0	****	0	****		
****	****	****	****	****	0	****	U	4.4.4.4.4.	-	-
nsity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
****	****	****	****	****	0	****	_	ale ale ale ale ale		
****	****	****	****	****	0	****	0	****	-	-
nsity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
****	****	****	****	****	0	****	_	ale ale ale ale ale		
****	****	****	****	****	0	****	0	****	-	-
					Overall					
s										
s 34,273	****	****	****	****	2.02	****	0.92	****	1.89 (0.94, 3.77)	0.073
	13 15 ensity Score Ma ***** ensity Score Ma 11 12 s ***** ensity Score Ma ***** ensity Score Ma *****	New Users at Risk	Number of Years Days At Risk At Risk 13	Person Person Person Number of Years Days Years New Users at Risk at Risk at Risk at Risk 13	Person Person Person Number Number Years Days Years Of New Users at Risk at Risk at Risk Events	Person Person Person Person Number 1,000 Number of Years Days Years of Person New Users at Risk at Risk at Risk Events Years	Number of Years Days Years Of Person Number of Years Days Years Of Person New Users	Number of Years Days Years O Person Number of Years Days Years At Risk Events Years New Users Vears At Risk Events Years New Users Table 270 Days Years Ye	Number of Person Person Person Person Person Number 1,000 Risk per Person 1,000 Pers	Number of Person Person Person Person Person Person Number of Person Person Person Person Person Person Number of Person Person Person Number of Person Person Number of Pers

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	26,475	****	****	****	****	2.07	****	1.45	****	3.33 (0.92, 12.11)	0.067
SV	26,475	****	****	****	****	0.62	****	1.45		3.33 (0.92, 12.11)	0.067
Fixed Ratio 1:1 Prope	ensity Score Mat	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ACEI-SV 14-day	26,475	****	****	****	****	2.12	****	1.21	****	2.30 (1.04, 5.09)	0.04
SV	26,475	****	****	****	****	0.92	****	1.21		2.30 (1.04, 3.09)	0.04
					0 -	- 30 Days					
Site-Adjusted Analysis	is										
ACEI-SV 14-day	34,273	****	****	****	****	2.79	****	1.53	****	2.25 (0.58, 8.72)	0.239
SV	30,126	****	****	****	****	1.25	****	1.55		2.23 (0.36, 6.72)	0.239
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	26,475	****	****	****	****	3.72	****	2.66	****	2 50 / 0 72 16 95\	0.110
SV	26,475	****	****	****	****	1.06	****	2.66		3.50 (0.73, 16.85)	0.118
			l:4: l A	nalusia. Cali	nor- 0 OF						
Fixed Ratio 1:1 Prope	ensity Score Mar	tched Unco	onditional A	naiysis; caii	per – 0.05						
Fixed Ratio 1:1 Prope ACEI-SV 14-day	ensity Score Mat 26,475	****	****	****	*****	3.61	****	2.10	****	2 56 / 0 66 0 00)	0.172
•					•	3.61 1.42	****	2.19	****	2.56 (0.66, 9.90)	0.173
ACEI-SV 14-day	26,475	****	****	****	*****			2.19	****	2.56 (0.66, 9.90)	0.173
ACEI-SV 14-day	26,475 26,475	****	****	****	*****	1.42	****	2.19	****	2.56 (0.66, 9.90)	0.173
ACEI-SV 14-day SV	26,475 26,475	****	****	****	*****	1.42			****		
ACEI-SV 14-day SV Site-Adjusted Analysis ACEI-SV 14-day SV	26,475 26,475 is 26,652 27,490	*****	*****	*****	***** 31 ***** *****	1.42 - 60 Days	****	2.19		2.56 (0.66, 9.90) 1.69 (0.40, 7.06)	0.173
ACEI-SV 14-day SV Site-Adjusted Analysis ACEI-SV 14-day SV	26,475 26,475 is 26,652 27,490	*****	*****	*****	***** 31 ***** *****	1.42 - 60 Days 2.76	****				
ACEI-SV 14-day SV Site-Adjusted Analysis ACEI-SV 14-day	26,475 26,475 is 26,652 27,490	*****	*****	*****	***** 31 ***** *****	1.42 - 60 Days 2.76	****	1.14	****		
ACEI-SV 14-day SV Site-Adjusted Analysis ACEI-SV 14-day SV Fixed Ratio 1:1 Prope	26,475 26,475 is 26,652 27,490 ensity Score Mar	***** **** ***** tched Cond	***** ***** *****	***** ***** ***** !ysis; Calipe	***** 31 **** **** r= 0.05 ²	1.42 - 60 Days 2.76 1.61	****				
ACEI-SV 14-day SV Site-Adjusted Analysis ACEI-SV 14-day SV Fixed Ratio 1:1 Prope ACEI-SV 14-day	26,475 26,475 is 26,652 27,490 ensity Score Mar 18,856 18,856	***** **** **** tched Cond ***** *****	***** **** ditional Ana *****	***** ***** ***** lysis; Calipe *****	***** 31 ***** r= 0.05 ² ***** *****	1.42 - 60 Days 2.76 1.61	*****	1.14	****		
ACEI-SV 14-day SV Site-Adjusted Analysic ACEI-SV 14-day SV Fixed Ratio 1:1 Prope ACEI-SV 14-day SV	26,475 26,475 is 26,652 27,490 ensity Score Mar 18,856 18,856	***** **** **** tched Cond ***** *****	***** **** ditional Ana *****	***** ***** ***** lysis; Calipe *****	***** 31 ***** r= 0.05 ² ***** *****	1.42 - 60 Days 2.76 1.61	*****	1.14	****		

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	90 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	18,105	****	****	****	****	2.98	****	1.53	****	2.05 (0.38, 11.19)	0.407
SV	18,275	****	****	****	****	1.45	****	1.55		2.03 (0.38, 11.19)	0.407
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	8,519	****	****	****	****	0	****	4.72	****		
SV	8,519	****	****	****	****	1.72	****	-1.72	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	13,847	****	****	****	****	0.98	****	0.16	****	4 20 / 0 07 40 44)	0.000
SV	16,209	****	****	****	****	0.82	****	0.16	****	1.20 (0.07, 19.14)	0.899
	·				91	- 180 Days					
Site-Adjusted Analys	sis										
ACEI-SV 14-day	14,508	****	****	****	****	0.71	****	0.42	****	0.62 (0.44 . 2.70)	0.647
SV	15,017	****	****	****	****	1.13	****	-0.42	****	0.63 (0.11, 3.79)	0.617
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lvsis: Calipe	r= 0.05 ²						
ACEI-SV 14-day	5,593	****	****	****	****	0	****	_	4.4.4.4		
SV	5,593	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalysis; Cal	iper= 0.05						
ACEI-SV 14-day	11,032	****	****	****	****	0.94	****		ale ale ale ale		
SV	13,380	****	****	****	****	1.26	****	-0.32	****	0.74 (0.12, 4.46)	0.747
	2,222				181	- 270 Days					
Site-Adjusted Analys	sis					,					
ACEI-SV 14-day	9,357	****	****	****	****	2.07	****	2.07	****		
SV	8,235	****	****	****	****	0	****	2.07	****	-	-
Fixed Ratio 1:1 Prop		tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ACEI-SV 14-day	2,006	****	****	****	****	0	****	_	ale ale ale ale		
SV	2,006	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ACEI-SV 14-day	6,969	****	****	****	****	2.12	****	0.10	****		
SV	7,446	****	****	****	****	0	****	2.12	ጥጥጥጥ	-	-

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Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

							Incidence			
					Incidence		Rate	Difference		
		Average	Average		Rate per		Difference	in		
	Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
				271	- 365 Days					
is										
6,657	****	****	****	****	1.35	****	0.42	****	1 44 / 0 12 15 07\	0.767
5,147	****	****	****	****	0.92	****	0.45		1.44 (0.15, 15.67)	0.767
ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
901	****	****	****	****	0	****	0	****		
901	****	****	****	****	0	****	U		-	-
ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
4,821	****	****	****	****	1.9	****	0.0	****	1.06 / 0.17. 20.52\	0.612
4,709	****	****	****	****	0.99	****	0.9		1.80 (0.17, 20.53)	
	6,657 5,147 ensity Score Mar 901 901 ensity Score Mar 4,821	Number of New Users at Risk is 6,657 ***** 5,147 ***** ensity Score Matched Conc 901 ***** 901 ***** ensity Score Matched Unco 4,821 *****	Number of Years Days At Risk at Risk is 6,657 ***** ***** 6,657 ***** ***** 1,147 ***** ***** 2,147 ***** ***** 2,147 **** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 2,147 ***** ***** 3,147 ***** ***** 4,821 ***** *****	Person Person Person Number of Years Days Years New Users at Risk at Risk at Risk at Risk 6,657 ***** **** ***** 5,147 ***** **** ***** ensity Score Matched Conditional Analysis; Caliped 901 ***** **** ***** ensity Score Matched Unconditional Analysis; Caliped 901 ***** **** ***** ensity Score Matched Unconditional Analysis; Caliped 901 ***** **** *****	Person Person Person Number Number of Years Days Years Of New Users at Risk at Risk at Risk Events	Average Average Rate per	Average Average Rate per	Number of Years Days Years O Person New Users Vears S,147 Vears Vears Vears Vears Vears Vears Vears Vears O Vear	Number of Years Days Years O Person New Users S S S S S S S S S	Number of Years Days Years Days Years Days Years Days Years Days Days

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
						Overall					
Site-Adjusted Analy	rsis										
ARB-SV 14-day	35,088	****	****	****	****	3.28	****	1.04	****	2.40/1.46 4.25\	<0.001
SV	44,361	****	****	****	****	1.33	****	1.94		2.49 (1.46, 4.25)	<0.001
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	32,174	****	****	****	****	4.53	****	2.06	****	2.00 / 4.25 (.46)	0.000
SV	32,174	****	****	****	****	1.57	****	2.96	4. 4. 4. 4. 4.	2.89 (1.35, 6.16)	0.006
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	32,174	****	****	****	****	3.28	****	1.02	****	2.45 / 1.26 . 4.42)	0.003
SV	32,174	****	****	****	****	1.36	****	1.92		2.45 (1.36, 4.43)	0.003
					0	- 30 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	35,088	****	****	****	****	5.11	****	2.07	****	4 47 / 1 46 12 71\	0.009
SV	44,361	****	****	****	****	1.14	****	3.97		4.47 (1.46, 13.71)	0.009
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	32,174	****	****	****	****	5.29	****	2.07	****	4.00 / 4.42 44.47\	0.022
SV	32,174	****	****	****	****	1.32	****	3.97	4. 4. 4. 4. 4.	4.00 (1.13, 14.17)	0.032
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	32,174	****	****	****	****	5.13	****	2.00	****	4 24 / 4 22 45 20\	0.024
SV	32,174	****	****	****	****	1.17	****	3.96	nen nen nen nen	4.31 (1.22, 15.29)	0.024
					31	- 60 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	26,678	****	****	****	****	3.87	****	2.39	****	2.59 (0.76, 8.83)	0.13
SV	40,380	****	****	****	****	1.47	****	2.33		2.33 (0.70, 0.83)	0.15

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Table 17. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

· •	Number of	Person Years	Average Person Days	Average Person Years	Number of	Incidence Rate per 1,000 Person	Risk per 1,000	Incidence Rate Difference per 1,000 Person	Difference in Risk per 1,000	Hazard Ratio (95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²					·	
ARB-SV 14-day	22,573	****	****	****	****	4.62	****	2.00	****	2.00 / 0.64 .44.06\	0.470
SV	22,573	****	****	****	****	1.54	****	3.08	****	3.00 (0.61, 14.86)	0.178
ixed Ratio 1:1 Prop		tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	24,555	****	****	****	****	4.2	****	2.00	****	2 70 / 0 72 40 76	0.120
SV	29,561	****	****	****	****	1.51	****	2.69	nen nen nen nen	2.78 (0.72, 10.76)	0.138
					61	- 90 Days					
ite-Adjusted Analy	sis										
ARB-SV 14-day	17,947	****	****	****	****	3.77	****	1.76	****	1.80 (0.48, 6.70)	0.382
SV	26,440	****	****	****	****	2.02	****	1.70		1.80 (0.48, 0.70)	0.362
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	10,134	****	****	****	****	5.78	****	4.34	****	4.00 (0.45, 35.79)	0.215
SV	10,134	****	****	****	****	1.45	****	4.54		4.00 (0.45, 55.79)	0.215
ixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	16,557	****	****	****	****	4.09	****	2.05	****	1.98 (0.47, 8.27)	0.351
SV	19,509	****	****	****	****	2.04	****	2.03		1.38 (0.47, 8.27)	0.331
					91	- 180 Days					
Site-Adjusted Analy											
ARB-SV 14-day	14,275	****	****	****	****	2.57	****	0.97	****	1.68 (0.56, 5.02)	0.357
SV	21,443	****	****	****	****	1.6	****				
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana		r= 0.05 ²						
ARB-SV 14-day	6,661	****	****	****	****	4.29	****	2.14	****	2.00 (0.37, 10.92)	0.423
SV	6,661	****	****	****	****	2.14	****	2.14		2.00 (0.37, 10.32)	0.423
ixed Ratio 1:1 Prop											
ARB-SV 14-day	13,165	****	****	****	****	2.79	****	1.37	****	2.01 (0.59, 6.90)	0.264
SV	16,012	****	****	****	****	1.42	****	1.57		2.01 (0.33, 0.30)	0.204
					181	- 270 Days					
ite-Adjusted Analy											
ARB-SV 14-day	8,980	****	****	****	****	2.18	****	1.29	****	2.33 (0.43, 12.71)	0.329
SV	11,557	****	****	****	****	0.89	****	1.23		2.33 (0.73, 12.71)	0.525

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Table 17. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Risk Window

Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ² ARB-SV 14-day 2,297 ***** ***** ***** 0 ***** 2.71 ***** -2.71 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ARB-SV 14-day 8,256 ***** ***** ***** 1.78 ***** 0.61 ***** 1.52 (0.2 ****** 1.17 ****** 1.17	l Ratio nfidence Wald val) ¹ P-Value ¹
SV 2,297 ***** **** **** **** 2.71 ***** Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ARB-SV 14-day 8,256 ***** **** ***** 1.78 ***** SV 8,794 ***** **** ***** 1.17 ***** 0.61 ***** 1.52 (0.2)	
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 ARB-SV 14-day 8,256 ***** ***** ***** 1.78 ***** 0.61 ***** 1.52 (0.2	_
ARB-SV 14-day 8,256 **** **** **** 1.78 **** 0.61 **** 1.52 (0.2	· -
SV 8,794 **** **** **** 1.17 **** 0.61 ***** 1.52 (0.2	
SV 8,794 **** **** **** 1.17 ****	35 0.00\ 0.640
	25, 9.08) 0.648
271 - 365 Days	
Site-Adjusted Analysis	
ARB-SV 14-day 6,253 ***** ***** ***** 1.47 ***** 0.82 ***** 2.12 (0.1	0.22.50) 0.527
SV 7,227 **** **** **** 0.65 **** 0.82 ***** 2.13 (0.1	.9, 23.50) 0.537
Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05 ²	
ARB-SV 14-day 999 ***** ***** ***** 0 *****	
SV 999 ***** ***** ***** 0 *****	-
Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05	
ARB-SV 14-day 5,732 ***** ***** ***** 0.81 *****	0.000
SV 5,571 ***** **** **** 0.84 **** -0.03 ***** 0.95 (0.0	06, 15.12) 0.969

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 (ARB) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
No Angioedema (-18	83, -1)										
						Overall					
Site-Adjusted Analy	sis										
ARB-SV 14-day	35,055	****	****	****	****	2.93	****	1.85	****	2.77 (1.55, 4.97)	<0.001
SV	44,301	****	****	****	****	1.08	****	1.05		2.77 (1.55, 4.57)	\0.001
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	32,130	****	****	****	****	3.84	****	2.62	****	3.14 (1.34, 7.36)	0.008
SV	32,130	****	****	****	****	1.22	****	2.02		3.14 (1.34, 7.30)	0.008
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	32,130	****	****	****	****	2.91	****	1.8	****	2.69 (1.41, 5.15)	0.003
SV	32,130	****	****	****	****	1.11	****	1.0		2.09 (1.41, 3.13)	0.003
					0	- 30 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	35,055	****	****	****	****	3.54	****	2.97	****	6.32 (1.36, 29.26)	0.018
SV	44,301	****	****	****	****	0.57	****	2.37		0.32 (1.30, 23.20)	0.018
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	32,130	****	****	****	****	3.53	****	2.65	****	4.00 (0.85, 18.84)	0.08
SV	32,130	****	****	****	****	0.88	****	2.03		4.00 (0.65, 16.64)	0.08
Fixed Ratio 1:1 Prop	ensity Score Ma			nalysis; Cal	iper= 0.05						
ARB-SV 14-day	32,130	****	****	****	****	3.43	****	2.64	****	4.39 (0.93, 20.68)	0.061
SV	32,130	****	****	****	****	0.78	****	2.04		7.55 (0.55, 20.06)	0.001
					31	- 60 Days					
Site-Adjusted Analy	sis						<u> </u>	<u> </u>	<u> </u>		
ARB-SV 14-day	26,657	****	****	****	****	3.87	****	2.39	****	2.58 (0.76, 8.83)	0.13
SV	40,327	****	****	****	****	1.48	****	2.33		2.30 (0.70, 0.03)	0.13

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Table 18. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	22,545	****	****	****	****	4.63	****	2.00	****	2.00 (0.64 .44.06)	0.470
SV	22,545	****	****	****	****	1.54	****	3.09	4. 4. 4. 4. 4.	3.00 (0.61, 14.86)	0.178
ixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	24,524	****	****	****	****	4.2	****	2.69	****	2 70 / 0 72 10 75\	0.120
SV	29,521	****	****	****	****	1.51	****	2.69		2.78 (0.72, 10.75)	0.138
					61	- 90 Days					
Site-Adjusted Analys	is										
ARB-SV 14-day	17,933	****	****	****	****	3.78	****	2.26	****	2.40 (0.57, 10.05)	0.23
SV	26,402	****	****	****	****	1.52	****	2.20		2.40 (0.57, 10.05)	0.23
ixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	10,118	****	****	****	****	5.79	****	4.24	****	4.00 (0.45, 25, 70)	0.245
SV	10,118	****	****	****	****	1.45	****	4.34		4.00 (0.45, 35.79)	0.215
ixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	16,536	****	****	****	****	4.1	****	2.73	****	2.06 / 0.59, 45, 29)	0.104
SV	19,481	****	****	****	****	1.36	****	2.73		2.96 (0.58, 15.28)	0.194
					91 -	- 180 Days					
Site-Adjusted Analys	is										
ARB-SV 14-day	14,263	****	****	****	****	2.57	****	1.24	****	2.04 (0.64, 6.47)	0.228
SV	21,412	****	****	****	****	1.33	****	1.24		2.04 (0.04, 6.47)	0.226
ixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	6,649	****	****	****	****	4.3	****	2.22	****	4.00 / 0.45 .25 .70\	0.215
SV	6,649	****	****	****	****	1.07	****	3.22	4. 4. 4. 4. 4.	4.00 (0.45, 35.79)	0.215
ixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
	42 4 47	****	****	****	****	2.79	****				
ARB-SV 14-day	13,147					2.75		1.73	****	2.70 (0.70, 10.48)	0.15

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Table 18. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio (95% Confidence	Wald
	Number of	Years	Days	Years	of 	Person	1,000	Person	1,000	•	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Site-Adjusted Analys	<u> </u>				181	270 Days					
	8,973	****	****	****	****	2.19	****				
ARB-SV 14-day	•	****	****	****	****		****	1.29	****	2.33 (0.43, 12.70)	0.329
SV	11,540					0.9					
Fixed Ratio 1:1 Prop		*****	****	iysis; Calipe	er= 0.05 *****		****				_
ARB-SV 14-day	2,294	****	****	****	****	0	****	-2.71	****	-	-
SV	2,294					2.71	****				
Fixed Ratio 1:1 Prop	<u>-</u>	tcned Unco	nditional A	naiysis; Cai	*****	4.70	****				
ARB-SV 14-day	8,246	****	****	****	****	1.78	****	0.61	****	1.52 (0.25, 9.08)	0.648
SV	8,778	****	****	****		1.17	****			, ,	
Cita Adimeted Analy	-1-				2/1	365 Days					
Site-Adjusted Analys		****	****	****	****	1.47	****				
ARB-SV 14-day	6,246	****	****	****	****	1.47	****	0.82	****	2.13 (0.19, 23.49)	0.537
SV	7,216					0.65	4. 4. 4. 4.				
Fixed Ratio 1:1 Prop											
ARB-SV 14-day	998	****	****	****	****	0	****	0	****	-	_
SV	998	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop					•						
ARB-SV 14-day	5,723	****	****	****	****	0.81	****	-0.03	****	0.95 (0.06, 15.11)	0.968
SV	5,562	****	****	****	****	0.84	****			(
Angioedema (-183, -	-1)					_ "					
	•					Overall					
Site-Adjusted Analys		4.4.4.4.4	de de de de d	de de de de d	de de de de d						
ARB-SV 14-day	33	****	****	****	****	390.63	****	215.65	****	1.96 (0.48, 8.02)	0.347
SV	60	****	****	****	****	174.98	****			== (===, ====,	

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Table 18. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

			Average	Average		Incidence Rate per		Incidence Rate Difference	Difference in		
		Person	Person	Person	Number	1,000	Dick nor	per 1,000	Risk per	Hazard Ratio	
	Number of				of	•	Risk per	. ,	-	(95% Confidence	Wald
NA - di - di Dun do et		Years	Days	Years		Person	1,000	Person	1,000	•	P-Value ¹
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-value
Fixed Ratio 1:1 Prop		tched Conc	****	lysis; Calipe	*****		****				
ARB-SV 14-day	22					835.65		557.1	****	3.00 (0.31, 28.84)	0.341
SV	22	****	****	****	****	278.55	****				
Fixed Ratio 1:1 Prop											
ARB-SV 14-day	22	****	****	****	****	571.43	****	302.61	****	1.86 (0.31, 11.19)	0.498
SV	22	****	****	****	****	268.82	****				
					0	- 30 Days					
Site-Adjusted Analys											
ARB-SV 14-day	33	****	****	****	****	1,860.47	****	1,440.30	****	4.17 (0.74, 23.58)	0.107
SV	60	****	****	****	****	420.17	****	2,110.00			0.107
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	22	****	****	****	****	2,272.73	****	1 515 15	****	2.00 / 0.21 .20 04\	0.341
SV	22	****	****	****	****	757.58	****	1,515.15		3.00 (0.31, 28.84)	0.541
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	22	****	****	****	****	2,205.88	****	1 (21 17	****	2.45 / 0.26 22.45\	0.304
SV	22	****	****	****	****	574.71	****	1,631.17		3.45 (0.36, 33.15)	0.284
					31	- 60 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	23	****	****	****	****	0	****	0	****		
SV	55	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	13	****	****	****	****	0	****	-	****		
SV	13	****	****	****	****	0	****	0	ተ ተ ተ ተ ተ	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	14	****	****	****	****	0	****		****		
SV	20	****	****	****	****	0	****	0	****	-	-

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Table 18. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

						Incidence		Incidence	D:#arara		
			A	A				Rate	Difference		
		_	Average	Average		Rate per		Difference	in	Hazard Ratio	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per		
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	14	****	****	****	****	0	****	-320.51	****	_	_
SV	42	****	****	****	****	320.51	****	-320.31		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	4.4.4.4.4	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****	-1041.67	****		
SV	13	****	****	****	****	1,041.67	****	-1041.67		-	-
					91	- 180 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	12	****	****	****	****	0	****	152.05	****		
SV	35	****	****	****	****	153.85	****	-153.85		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****	_	****		
SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****	_	ale ale ale ale		
SV	****	****	****	****	****	0	****	0	****	-	-
					181	- 270 Days					
Site-Adjusted Analys	sis					/					
ARB-SV 14-day	****	****	****	****	****	0	****		****		
SV	21	****	****	****	****	0	****	0	ተ ተ ተ ተ ተ	-	-

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Table 18. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, 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 Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	· Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²					•	
ARB-SV 14-day	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	****	-	-
					271	- 365 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	16	****	****	****	****	0	****	0	4 4 4 4	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****		****		
SV	****	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	and the state of	-	-

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

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²Conditional analysis accounts for informative events and person-time.

^{*****}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 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
			_			Incidence		Rate	Difference		
		_	Average	Average		Rate per		Difference	in	Hanned Batin	
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	144 1 1
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Unknown											
<u> </u>	•					Overall					
Site-Adjusted Analys		****	****	****	****		****				
ARB-SV 14-day	5,599	****	****	****	****	1.71	****	0.96	****	2.37 (0.38, 14.70)	0.354
SV	7,272					0.75	****				
Fixed Ratio 1:1 Prop		tched Cond	ditional Ana	lysis; Calipe							
ARB-SV 14-day	4,778	****	****	****	****	2.43	****	2.43	****	-	_
SV	4,778	****	****	****	****	0	****	2.10			
Fixed Ratio 1:1 Prop	•				•						
ARB-SV 14-day	4,778	****	****	****	****	1.33	****	0.77	****	2.59 (0.23, 28.82)	0.439
SV	4,778	****	****	****	****	0.56	****			2.03 (0.23, 20.02)	
					0	- 30 Days					
Site-Adjusted Analy											
ARB-SV 14-day	5,599	****	****	****	****	5.08	****	5.08	****	_	_
SV	7,272	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	4,778	****	****	****	****	3.08	****	3.08	****	_	_
SV	4,778	****	****	****	****	0	****	3.08		_	
Fixed Ratio 1:1 Prop	ensity Score Ma		onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	4,778	****	****	****	****	2.98	****	2.98	****	_	_
SV	4,778	****	****	****	****	0	****	2.30		<u>-</u>	
					31	- 60 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	3,983	****	****	****	****	0	****	0	****	_	_
SV	6,558	****	****	****	****	0	****	U		_	_

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	3,097	****	****	****	****	0	****	0	****		
SV	3,097	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	3,394	****	****	****	****	0	****	0	****		
SV	4,349	****	****	****	****	0	****	0		-	-
					61	- 90 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	2,676	****	****	****	****	0	****	-3.02	****	_	_
SV	4,423	****	****	****	****	3.02	****	-3.02			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	1,408	****	****	****	****	0	****	0	****		
SV	1,408	****	****	****	****	0	****	0	4. 4. 4. 4. 4.	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	2,292	****	****	****	****	0	****	<i>1</i> EE	****		
SV	2,930	****	****	****	****	4.55	****	-4.55		-	-
					91	- 180 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	2,116	****	****	****	****	2.42	****	0.88	****	2.44 (0.15, 39.11)	0.527
SV	3,574	****	****	****	****	1.54	****	0.00		2.44 (0.15, 59.11)	0.527
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	916	****	****	****	****	7.1	****	7.1	****		
SV	916	****	****	****	****	0	****	7.1		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	1,814	****	****	****	****	2.8	****	2.0	****		
SV	2,382	****	****	****	****	0	****	2.8		-	-

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						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	· Interval) ¹	P-Value ¹
THE GREAT THE GR	itell Oscio	ut mon	GC THISK	ut mon		270 Days	THE USE IS		11011 03013	ec. va.,	
Site-Adjusted Analys	sis										
ARB-SV 14-day	1,359	****	****	****	****	0	****	_	****		
SV	2,036	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lvsis: Calipe	r= 0.05 ²						
ARB-SV 14-day	364	****	****	****	****	0	****		****		
SV	364	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	1,179	****	****	****	****	0	****	0	****		
SV	1,384	****	****	****	****	0	****	0		-	-
					271	365 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	933	****	****	****	****	0	****	0	****		
SV	1,291	****	****	****	****	0	****	0			_
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	152	****	****	****	****	0	****	0	****		
SV	152	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	803	172.13	78.29	0.21	0	0	****	0	****		
SV	891	193.31	79.24	0.22	0	0	****				
Race: American Indi	an										
						Overall					
Site-Adjusted Analys											
ARB-SV 14-day	81	****	****	****	****	0	****	0	****	-	_
SV	145	****	****	****	****	0	****	J			

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²					-	
ARB-SV 14-day	66	****	****	****	****	0	****	0	****		
SV	66	****	****	****	****	0	****	0	40 40 40 40	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	66	****	****	****	****	0	****	0	****		
SV	66	****	****	****	****	0	****	0	de de de de de	-	-
					0	- 30 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	81	****	****	****	****	0	****	0	****	_	_
SV	145	****	****	****	****	0	****	0		_	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	66	****	****	****	****	0	****	0	****		
SV	66	****	****	****	****	0	****	0	4-4-4-4-4	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	66	****	****	****	****	0	****	0	****		
SV	66	****	****	****	****	0	****	U		-	
					31	- 60 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	57	****	****	****	****	0	****	0	****		
SV	129	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	43	****	****	****	****	0	****	0	****		
SV	43	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	49	****	****	****	****	0	****	0	****		
SV	60	****	****	****	****	0	****	U		-	-

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								Incidence	D:W		
			A	A		Incidence		Rate	Difference		
		Davasa	Average	Average	Niaha	Rate per	Dial	Difference	in Dialoman	Hazard Ratio	
	Nissan and	Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	(95% Confidence	Wald
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	•	
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Site-Adjusted Analys	ale.				91	- 90 Days					
ARB-SV 14-day	33	****	****	****	****	0	****				
SV	33 87	****	****	****	****	0	****	0	****	-	-
	_	tabad Cana	ditional Ana	lucia. Calina	0 0F ²	<u> </u>					
Fixed Ratio 1:1 Prop	16	*****	*****	****	*****	0	****				
SV	16	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	===	tched Unco	nditional A	nalysis: Cali	iner- 0 05						
ARB-SV 14-day	26	****	****	****	****	0	****				
SV	36	****	****	****	****	0	****	0	****	-	-
31	30				91	- 180 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	29	****	****	****	****	0	****		****		
SV	66	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	13	****	****	****	****	0	****	•	****		
SV	13	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	24	****	****	****	****	0	****	0	****		
SV	29	****	****	****	****	0	****	U		-	-
					181	- 270 Days					
Site-Adjusted Analys											
ARB-SV 14-day	16	****	****	****	****	0	****	0	****	_	_
SV	33	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop					r= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****	_	_
SV	****	****	****	****	****	0	****			· 	
Fixed Ratio 1:1 Prop	-				•						
ARB-SV 14-day	12	****	****	****	****	0	****	0	****	-	_
SV	13	****	****	****	****	0	****	Ŭ			

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					271	- 365 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	12	****	****	****	****	0	****	0	****		
SV	19	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	the de de de de	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	U		-	-
Race: Asian											
						Overall					
Site-Adjusted Analy	sis										
ARB-SV 14-day	847	****	****	****	****	3.86	****	3.86	****	_	_
SV	532	****	****	****	****	0	****	3.80			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	452	****	****	****	****	0	****	0	****		
SV	452	****	****	****	****	0	****	U		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	452	****	****	****	****	0	****	0	****		
SV	452	****	****	****	****	0	****	U		-	-

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					0	- 30 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	847	****	****	****	****	0	****	0	****	_	_
SV	532	****	****	****	****	0	****				
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	452	****	****	****	****	0	****	0	****	_	
SV	452	****	****	****	****	0	****	0			
ixed Ratio 1:1 Prop	ensity Score Ma			•	•						
ARB-SV 14-day	452	****	****	****	****	0	****	0	****	_	_
SV	452	****	****	****	****	0	****				
					31	60 Days					
Site-Adjusted Analys											
ARB-SV 14-day	587	****	****	****	****	0	****	0	****	-	_
SV	490	****	****	****	****	0	****				
ixed Ratio 1:1 Prop											
ARB-SV 14-day	295	****	****	****	****	0	****	0	****	_	_
SV	295	****	****	****	****	0	****				
ixed Ratio 1:1 Prop					•						
ARB-SV 14-day	318	****	****	****	****	0	****	0	****	-	_
SV	418	****	****	****	****	0	****				
					61	90 Days					
Site-Adjusted Analys		****	****	****	****		****				
ARB-SV 14-day	393	****	****	****	****	0	****	0	****	-	-
SV	334					0	40 40 40 40				
ixed Ratio 1:1 Prop							ale ale ale ale				
ARB-SV 14-day	146	****	****	****	****	0	****	0	****	-	-
SV	146					0	****				
Fixed Ratio 1:1 Prop	•	tched Unco	nditional A	nalysis; Cal	iper= 0.05 ****		****				
ARB-SV 14-day	219	****	****	****	****	0	****	0	****	-	-
SV	293	ጥጥጥ	ጥጥጥ	ጥጥጥ	ተተተ ተ	0	****				

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

		Person	Average Person	Average Person	Number	Incidence Rate per 1,000	Risk per	Rate Difference per 1,000	Difference in Risk per	Hazard Ratio	Mr-14
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					91	- 180 Days					
ite-Adjusted Analys		****	****	****	****		****				
ARB-SV 14-day	309	****	****	****	****	0	****	0	****	-	_
SV	256					0	****				
ixed Ratio 1:1 Prop											
ARB-SV 14-day	85	****	****	****	****	0	****	0	****	_	_
SV	85	****	****	****	****	0	****				
ixed Ratio 1:1 Prop	ensity Score Ma				•						
ARB-SV 14-day	165	****	****	****	****	0	****	0	****	_	_
SV	221	****	****	****	****	0	****	0		_	
					181	270 Days					
Site-Adjusted Analys	is										
ARB-SV 14-day	207	****	****	****	****	24.17	****	24.17	****		
SV	138	****	****	****	****	0	****	24.17		-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	33	****	****	****	****	0	****		****		
SV	33	****	****	****	****	0	****	0	****	-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	116	****	****	****	****	0	****		****		
SV	116	****	****	****	****	0	****	0	****	-	-
					271	365 Days					
ite-Adjusted Analys	is										
ARB-SV 14-day	134	****	****	****	****	0	****		****		
SV	88	****	****	****	****	0	****	0	~ ~ ~ ~ ~	-	-
ixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lvsis: Calipe	r= 0.05 ²						
ARB-SV 14-day	14	****	****	****	****	0	****				
SV	14	****	****	****	****	0	****	0	****	-	-
ixed Ratio 1:1 Prop		tched Unco	nditional A	nalvsis: Cali	iper= 0.05						
ARB-SV 14-day	70	****	****	****	****	0	****		****		
								0			

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
						Overall					
Site-Adjusted Analy	sis										
ARB-SV 14-day	4,731	****	****	****	****	5.14	****	1.2	****	1.30 (0.45, 3.71)	0.628
SV	5,990	****	****	****	****	3.94	****	1.2		1.30 (0.43, 3.71)	0.028
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	4,182	****	****	****	****	8	****	4.8	****	2.50 (0.49, 12.89)	0.273
SV	4,182	****	****	****	****	3.2	****	4.0		2.30 (0.43, 12.63)	0.273
Fixed Ratio 1:1 Prop	ensity Score Ma										
ARB-SV 14-day	4,182	****	****	****	****	5.06	****	0.4	****	1.11 (0.36, 3.43)	0.862
SV	4,182	****	****	****	****	4.65	****	0.4		1.11 (0.30, 3.43)	0.002
					0	- 30 Days					
Site-Adjusted Analy											
ARB-SV 14-day	4,731	****	****	****	****	8.81	****	6.7	****	4.07 (0.42, 39.15)	0.224
SV	5,990	****	****	****	****	2.11	****				
Fixed Ratio 1:1 Prop	ensity Score Ma										
ARB-SV 14-day	4,182	****	****	****	****	10.26	****	6.84	****	3.00 (0.31, 28.84)	0.341
SV	4,182	****	****	****	****	3.42	****				
Fixed Ratio 1:1 Prop	•				•						
ARB-SV 14-day	4,182	****	****	****	****	9.96	****	6.95	****	3.19 (0.33, 30.63)	0.316
SV	4,182	****	****	****	****	3.01	****				
Cita Adinatad And	-:-				31	60 Days					
Site-Adjusted Analy		****	****	****	****	4.22	****				
ARB-SV 14-day	3,528	****	****	****	****	4.32	****	1.44	****	1.59 (0.10, 25.44)	0.743
SV	5,447					2.88	90 90 AT TE TE			· .	
Fixed Ratio 1:1 Prop		tched Cond					*****				
ARB-SV 14-day	2,863	****	****	****	****	6.55	****	6.55	****	-	-
SV	2,863					0	****				
Fixed Ratio 1:1 Prop	•	****	nditional A	nalysis; Cal	*****	4.0	****				
ARB-SV 14-day	3,123	****	****	****	****	4.9	****	0.83	****	1.28 (0.08, 20.43)	0.862
SV	3,840	11·11·11·11·11·11	~~~~~	~~~~~	~~~~~	4.07	~~~~~			•	

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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	Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% Confidence Interval) ¹	Wald P-Value ¹
					61	- 90 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	2,191	****	****	****	****	6.31	****	1.96	****	1.47 (0.09, 23.51)	0.785
SV	3,141	****	****	****	****	4.35	****	1.50		1.47 (0.05, 25.51)	0.765
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	1,029	****	****	****	****	14.68	****	14.60	****		
SV	1,029	****	****	****	****	0	****	14.68		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	per= 0.05						
ARB-SV 14-day	1,925	****	****	****	****	7.2	****	1 1 5	****	1 21 / 0 00 10 20\	0.892
SV	2,243	****	****	****	****	6.05	****	1.15		1.21 (0.08, 19.39)	0.892
					91	- 180 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	1,653	****	****	****	****	0	****	F 36	****		
SV	2,381	****	****	****	****	5.26	****	-5.26		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	613	****	****	****	****	0	****		****		
SV	613	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	nditional A	nalysis; Cali	per= 0.05						
ARB-SV 14-day	1,447	****	****	****	****	0	****		****		
SV	1,727	****	****	****	****	3.54	****	-3.54	****	-	-
	,				181	- 270 Days					
Site-Adjusted Analys	sis					-					
ARB-SV 14-day	939	****	****	****	****	5.19	****	4.50	****	0.55 / 0.05 - 6.04)	0.634
SV	1,080	****	****	****	****	9.78	****	-4.59	75 75 75 75 75	0.55 (0.05, 6.01)	0.621
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	litional Ana	lvsis: Calipe	r= 0.05 ²						
ARB-SV 14-day	161	****	****	****	****	0	****				
SV	161	****	****	****	****	36.95	****	-36.95	****	-	-
Fixed Ratio 1:1 Prop		tched Unco	nditional A	nalvsis: Cali	per= 0.05	23.33					
ARB-SV 14-day	804	****	****	****	****	6.04	****				
SV	824	****	****	****	****	12.82	****	-6.77	****	0.50 (0.05, 5.50)	0.57
	32.				271	- 365 Days					

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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) ¹	Wald P-Value ¹
Site-Adjusted Analy	sis										
ARB-SV 14-day	658	****	****	****	****	7.1	****	7.1	****		
SV	663	****	****	****	****	0	****	7.1		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	77	****	****	****	****	0	****	0	****		
SV	77	****	****	****	****	0	****	0	<i>ተተ</i> ቀቀ	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	567	****	****	****	****	0	****				
SV	507	****	****	****	****	0	****	0		-	-

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Race: Pacific Islande	r										
						Overall					
Site-Adjusted Analys											
ARB-SV 14-day	45	****	****	****	****	0	****	0	****	_	_
SV	46	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	29	****	****	****	****	0	****	0	****		
SV	29	****	****	****	****	0	****	0		-	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	29	****	****	****	****	0	****	0	****	_	_
SV	29	****	****	****	****	0	****				
					0	- 30 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	45	****	****	****	****	0	****	0	****	_	_
SV	46	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	29	****	****	****	****	0	****	0	****		
SV	29	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma										
ARB-SV 14-day	29	****	****	****	****	0	****	0	****	_	_
SV	29	****	****	****	****	0	****				
					31	- 60 Days					
Site-Adjusted Analys											
ARB-SV 14-day	37	****	****	****	****	0	****	0	****	_	_
SV	43	****	****	****	****	0	****	J			

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								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²					·	
ARB-SV 14-day	24	****	****	****	****	0	****		****		
SV	24	****	****	****	****	0	****	0	****	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	25	****	****	****	****	0	****	0	****		
SV	28	****	****	****	****	0	****	0		-	-
					61	- 90 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	23	****	****	****	****	0	****	0	****	_	_
SV	27	****	****	****	****	0	****	0		_	_
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	14	****	****	****	****	0	****	0	****		
SV	17	****	****	****	****	0	****	U		-	-
					91	- 180 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	13	****	****	****	****	0	****	0	****		
SV	25	****	****	****	****	0	****	<u> </u>		<u>-</u>	
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0	nen nen nen nen	-	-
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	16	****	****	****	****	0	****	U		-	-

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						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					181	- 270 Days				·	
Site-Adjusted Analys	sis										
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	14	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0		-	-
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Unco	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		_
SV	11	****	****	****	****	0	****	U		-	
					271	- 365 Days					
Site-Adjusted Analys											
ARB-SV 14-day	****	****	****	****	****	0	****	0	****	_	_
SV	****	****	****	****	****	0	****				
Fixed Ratio 1:1 Prope	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	U		-	
Fixed Ratio 1:1 Prope	•	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	****	****	****	****	****	0	****	0	****		
SV	****	****	****	****	****	0	****	0			
Race: White											
						Overall					
Site-Adjusted Analys											
ARB-SV 14-day	23,785	****	****	****	****	3.3	****	2.21	****	3.14 (1.59, 6.19)	<0.001
SV	30,376	****	****	****	****	1.09	****	2.21		3.11 (1.33, 0.13)	10.001

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

								Incidence			
						Incidence		Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	22,086	****	****	****	****	4.62	****	2.16	****	2.17 (1.26 7.02)	0.014
SV	22,086	****	****	****	****	1.46	****	3.16	4. 4. 4. 4. 4.	3.17 (1.26, 7.93)	0.014
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	22,086	****	****	****	****	3.54	****	2.50	****	2.75 / 1.70 .0.25\	0.001
SV	22,086	****	****	****	****	0.97	****	2.58		3.75 (1.70, 8.25)	0.001
					0 -	- 30 Days					
Site-Adjusted Analy											
ARB-SV 14-day	23,785	****	****	****	****	4.59	****	3.35	****	3.70 (0.98, 13.96)	0.053
SV	30,376	****	****	****	****	1.24	****	3.33		3.70 (0.38, 13.30)	0.055
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	22,086	****	****	****	****	5.09	****	2.02	****	4.00 / 0.05 10.04)	0.00
SV	22,086	****	****	****	****	1.27	****	3.82		4.00 (0.85, 18.84)	0.08
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cali	iper= 0.05						
ARB-SV 14-day	22,086	****	****	****	****	4.94	****	3.8	****	4.34 (0.92, 20.43)	0.064
SV	22,086	****	****	****	****	1.14	****	5.0		4.34 (0.92, 20.43)	0.064
					31	- 60 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	18,488	****	****	****	****	4.75	****	3.15	****	2.98 (0.75, 11.93)	0.122
SV	27,717	****	****	****	****	1.6	****	3.13		2.36 (0.73, 11.33)	0.122
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	r= 0.05 ²						
ARB-SV 14-day	15,838	****	****	****	****	5.43	****	4.34	****	E 00 / 0 E9 42 90\	0.142
SV	15,838	****	****	****	****	1.09	****	4.54		5.00 (0.58, 42.80)	0.142
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unc	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	17,208	****	****	****	****	5.1	****	4.37	****	7.05 (0.85, 58.55)	0.071
SV	20,332	****	****	****	****	0.72	****	4.57		7.03 (0.65, 56.55)	0.071

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

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) ¹	Wald P-Value ¹
					61	- 90 Days				•	
Site-Adjusted Analy	sis										
ARB-SV 14-day	12,635	****	****	****	****	4.27	****	2.83	****	2.99 (0.55, 16.35)	0.206
SV	18,438	****	****	****	****	1.44	****			2.33 (0.33, 10.33)	0.200
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	7,333	****	****	****	****	5.97	****	5.97	****		
SV	7,333	****	****	****	****	0	****			-	
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ARB-SV 14-day	11,797	****	****	****	****	4.57	****	3.61	****	4.75 (0.53, 42.46)	0.164
SV	13,673	****	****	****	****	0.96	****	3.01		4.73 (0.33, 42.40)	0.104
					91	- 180 Days					
Site-Adjusted Analy	sis										
ARB-SV 14-day	10,156	****	****	****	****	3.08	****	1.96	****	2.70 (0.67, 10.79)	0.16
SV	15,150	****	****	****	****	1.12	****	1.50		2.70 (0.07, 10.73)	0.10
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe							
ARB-SV 14-day	4,880	****	****	****	****	4.34	****	1.45	****	1.50 (0.25, 8.98)	0.657
SV	4,880	****	****	****	****	2.9	****	1.45		1.30 (0.23, 8.38)	0.037
Fixed Ratio 1:1 Prop	ensity Score Ma				•						
ARB-SV 14-day	9,486	****	****	****	****	3.31	****	1.82	****	2.22 (0.55, 8.88)	0.26
SV	11,393	****	****	****	****	1.49	****	1.02		2.22 (0.33, 0.00)	0.20
					181	- 270 Days					
Site-Adjusted Analy											
ARB-SV 14-day	6,454	****	****	****	****	1.52	****	1.52	****	-	-
SV	8,260	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	ensity Score Ma										
ARB-SV 14-day	1,738	****	****	****	****	0	****	0	****	_	_
SV	1,738	****	****	****	****	0	****				
Fixed Ratio 1:1 Prop	•										
ARB-SV 14-day	6,006	****	****	****	****	1.63	****	1.63	****	_	_
SV	6,300	****	****	****	****	0	****				

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Table 19. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Risk Window

						Incidence		Incidence Rate	Difference		
			Average	Average		Rate per		Difference	in		
		Person	Person	Person	Number	1,000	Risk per	per 1,000	Risk per	Hazard Ratio	
	Number of	Years	Days	Years	of	Person	1,000	Person	1,000	(95% Confidence	Wald
Medical Product	New Users	at Risk	at Risk	at Risk	Events	Years	New Users	Years	New Users	Interval) ¹	P-Value ¹
					271	- 365 Days					
Site-Adjusted Analys	sis										
ARB-SV 14-day	4,514	****	****	****	****	1.02	****	0.1	****	1.11 (0.07, 17.75)	0.941
SV	5,163	****	****	****	****	0.92	****				
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Cond	ditional Ana	lysis; Calipe	er= 0.05 ²						
ARB-SV 14-day	781	****	****	****	****	0	****	-7	****	-	-
SV	781	****	****	****	****	7	****	-/			
Fixed Ratio 1:1 Prop	ensity Score Ma	tched Unco	onditional A	nalysis; Cal	iper= 0.05						
ARB-SV 14-day	4,186	****	****	****	****	1.1	****	-0.08	****	0.94 (0.06, 15.00)	0.964
SV	3,984	****	****	****	****	1.18	****				

¹Data presented by a dash are unable to be calculated. This table may not use all data representations.

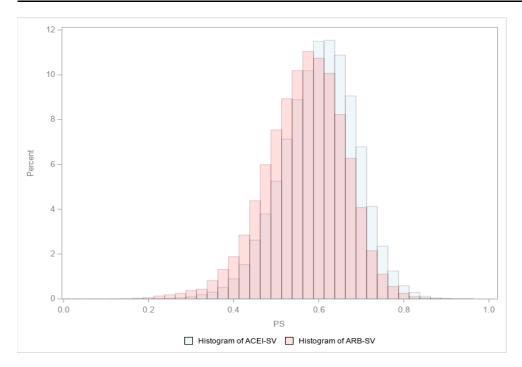
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²Conditional analysis accounts for informative events and person-time.

^{*****}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.



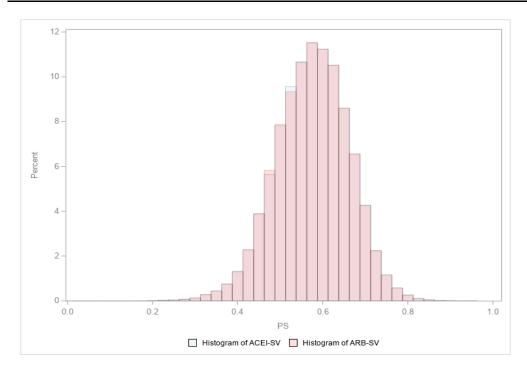
Figure 1a. Histogram of Propensity Score (PS) Distribution, Before Adjustment, Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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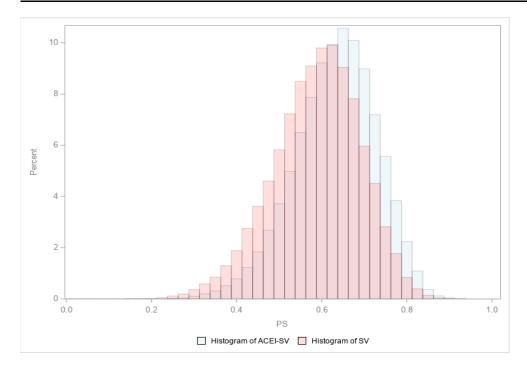
Figure 1b. Histogram of Propensity Score (PS) Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05 Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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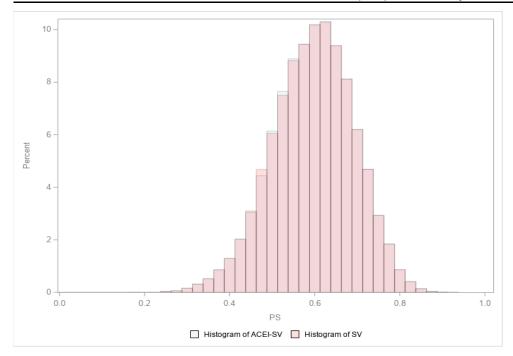
Figure 2a. Histogram of Propensity Score (PS) Distribution, Before Adjustment, Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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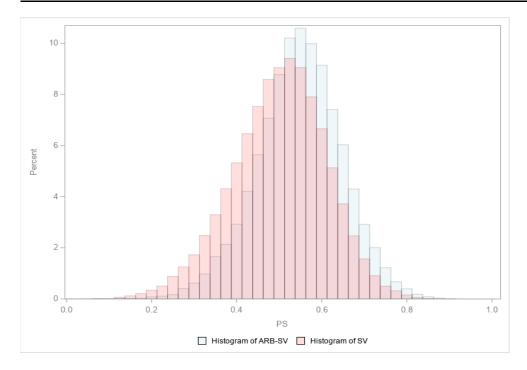
Figure 2b. Histogram of Propensity Score (PS) Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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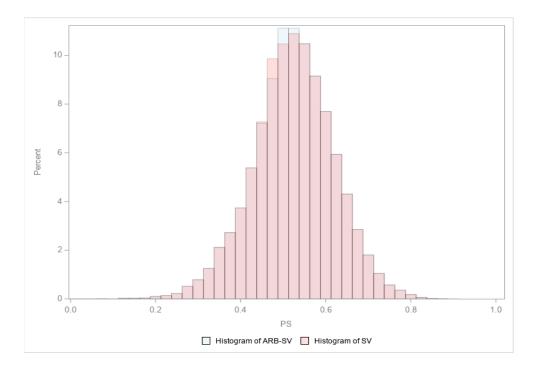
Figure 3a. Histogram of Propensity Score (PS) Distribution, Before Adjustment, Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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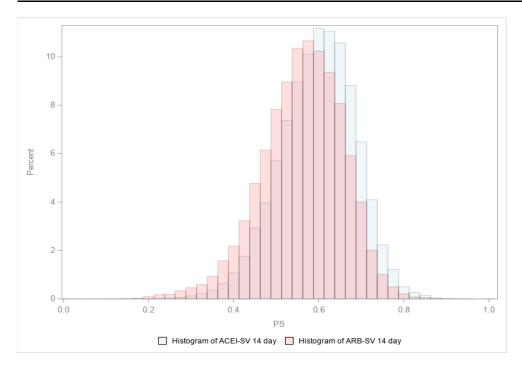
Figure 3b. Histogram for Propensity Score (PS) Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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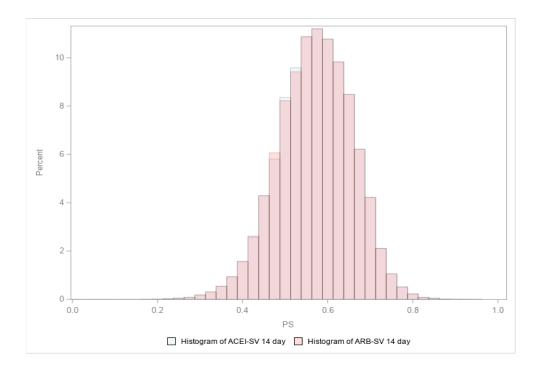
Figure 4a. Histogram of Propensity Score (PS) Distribution, Before Adjustment, Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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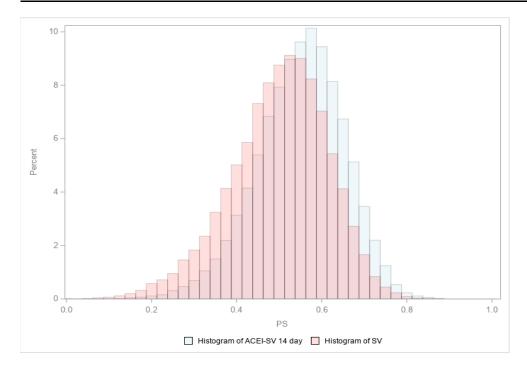
Figure 4b. Histogram for Propensity Score (PS) Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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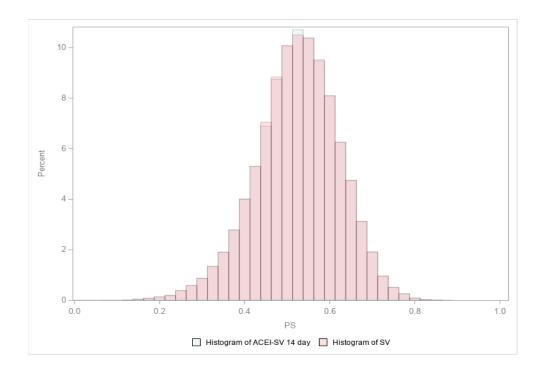
Figure 5a. Histogram of Propensity Score (PS) Distribution, Before Adjustment, Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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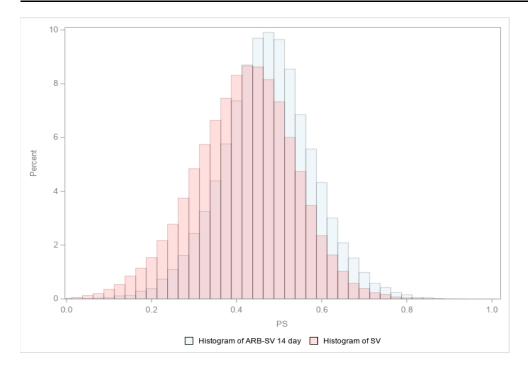
Figure 5b. Histogram for Propensity Score (PS) Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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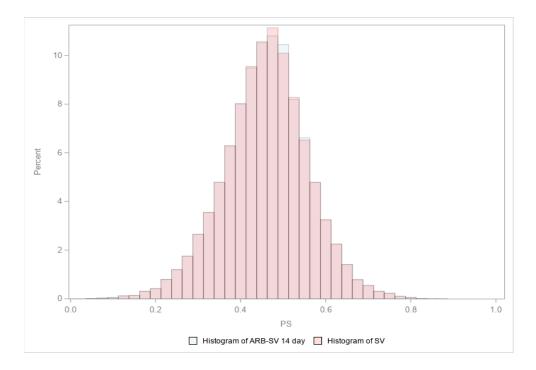
Figure 6a. Histogram of Propensity Score (PS) Distribution, Before Adjustment Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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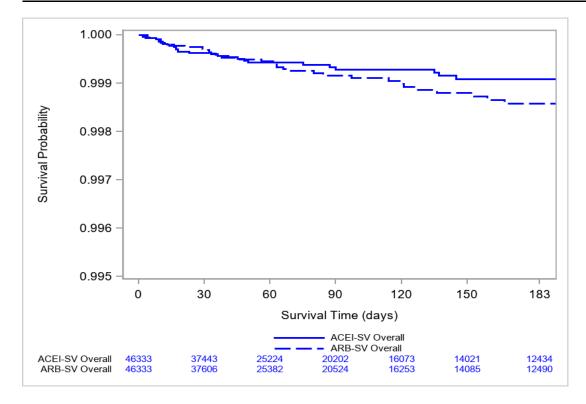
Figure 6b. Histogram of Propensity Score (PS) Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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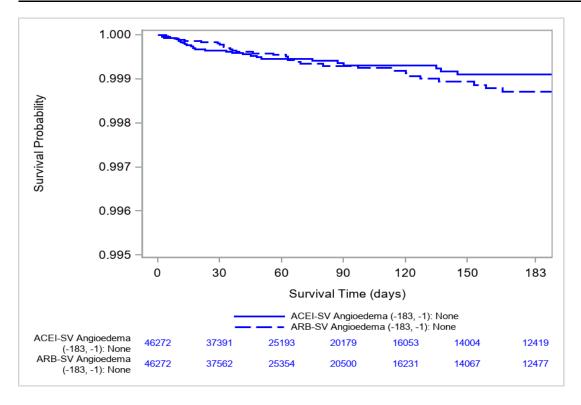
Figure 7a. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, Unconditional Propensity Score Matched Cohort in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Overall



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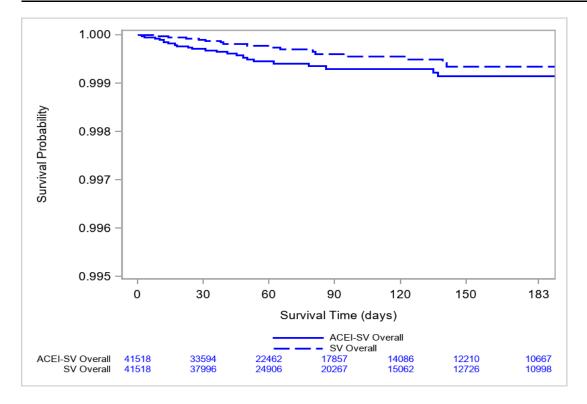
Figure 7b. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, Unconditional Propensity Score Matched Cohort, No Prior Angioedema (-183, -1) in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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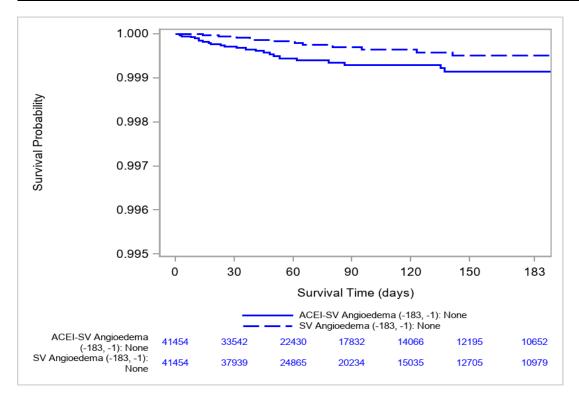
Figure 8a. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, Unconditional Propensity Score Matched Cohort in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Overall



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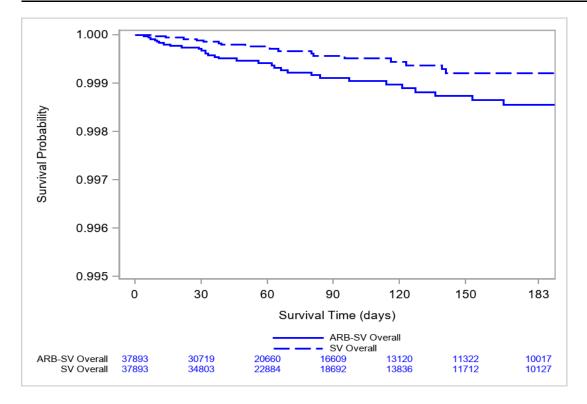
Figure 8b. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and New Initiators of SV, Unconditional Propensity Score Matched Cohort, No Prior Angioedema (-183, -1) in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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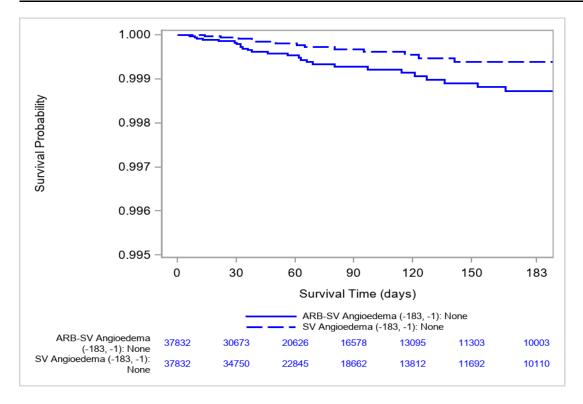
Figure 9a. Kaplan Meier Survival Curves for Risk of Angioedema Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, Unconditional Propensity Score Matched Cohort in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Overall



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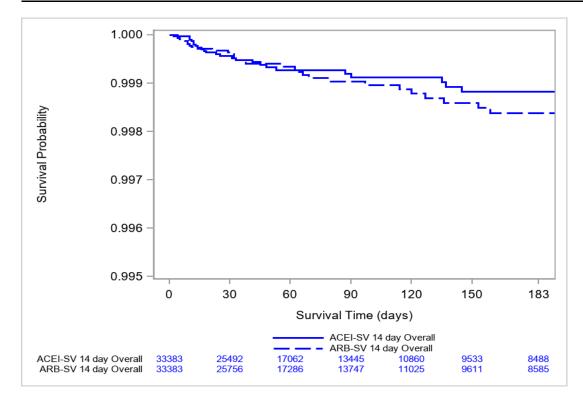
Figure 9b. Kaplan Meier Survival Curves for Risk of Angioedema Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 183 Days Prior, and New Initiators of SV, No Prior Angioedema (-183, -1) in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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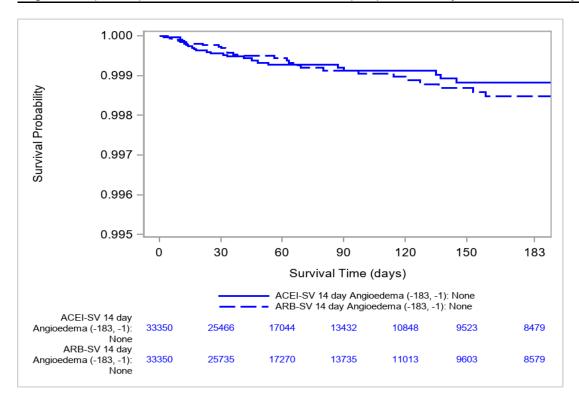
Figure 10a. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, Unconditional Propensity Score Matched Cohort in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Overall



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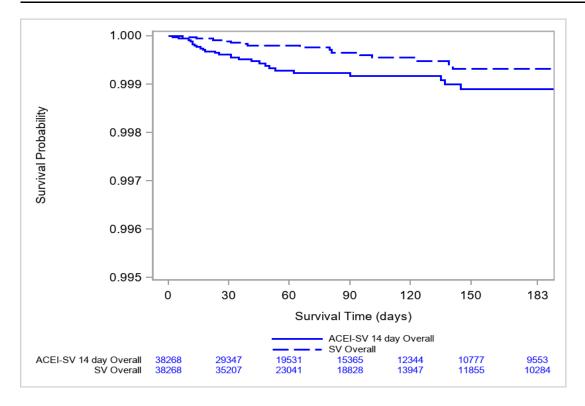
Figure 10b. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, Unconditional Propensity Score Matched Cohort, No Prior Angioedema (-183, -1) in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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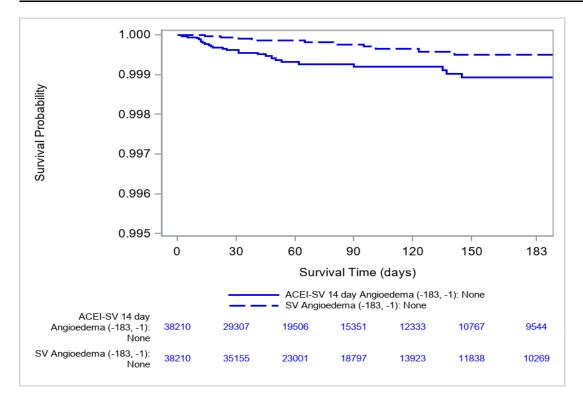
Figure 11a. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, Unconditional Propensity Score Matched Cohort in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Overall



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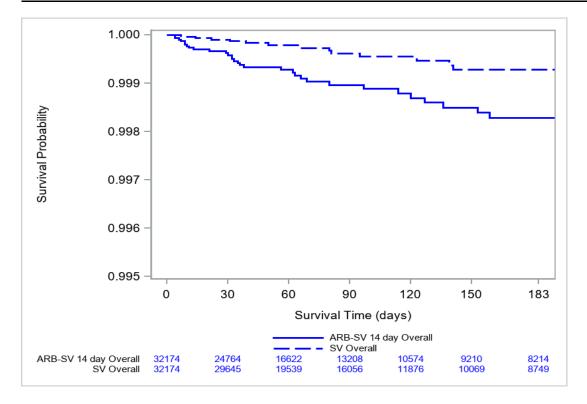
Figure 11b. Kaplan Meier Survival Curves for Risk of Angioedema Comparing New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and New Initiators of SV, Unconditional Propensity Score Matched Cohort, No Prior Angioedema (-183, -1) in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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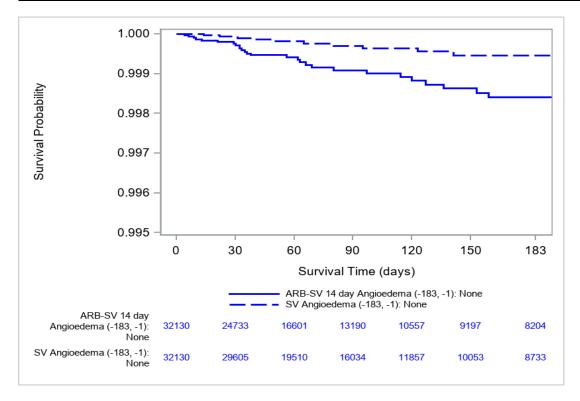
Figure 12a. Kaplan Meier Survival Curves for Risk of Angioedema Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, Unconditional Propensity Score Matched Cohort in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Overall



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Figure 12b. Kaplan Meier Survival Curves for Risk of Angioedema Comparing for New Initiators of Sacubitril/Valsartan (SV) with Use of Angiotensin II Receptor Blockers (ARB) in the 14 Days Prior, and New Initiators of SV, No Prior Angioedema (-183, -1) in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020



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Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (January 18, 2022)

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	1/1/2007	10/31/2019
DP05	1/1/2006	1/31/2020

 $^{^1}$ The start and end dates are based on available data at the time of cder_mpl2p_wp021_nsdp_v01 query execution

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Generic Name

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) Codes Used to Define Outcomes in this Request

		Code	
Code	Description	Category	Code Type
		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 Inclusion 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

lisinopril/hydrochlorothiazide lisinopril-hydrochlorothiazide

quinapril HClquinaprilramiprilramipriltrandolapriltrandolapril

Angiotensin II Receptor Blockers (ARB)

AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL Azor

AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL amlodipine-olmesartan

AMLODIPINE BESYLATE/VALSARTAN Exforge

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Appendix D. Generic and Brand Names of Medical Products Used to Define Inclusion and Exclusion Criteria in this Request			
Generic Name	Brand Name		
AMLODIPINE BESYLATE/VALSARTAN	amlodipine-valsartan		
AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE	Exforge HCT		
AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE	amlodipine-valsartan-hcthiazid		
AZILSARTAN MEDOXOMIL	Edarbi		
AZILSARTAN MEDOXOMIL/CHLORTHALIDONE	Edarbyclor		
CANDESARTAN CILEXETIL	Atacand		
CANDESARTAN CILEXETIL	candesartan		
CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE	Atacand HCT		
CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE	candesartan-hydrochlorothiazid		
EPROSARTAN MESYLATE	Teveten		
EPROSARTAN MESYLATE	eprosartan		
EPROSARTAN MESYLATE/HYDROCHLOROTHIAZIDE	Teveten HCT		
IRBESARTAN	Avapro		
IRBESARTAN	irbesartan		
IRBESARTAN/HYDROCHLOROTHIAZIDE	Avalide		
IRBESARTAN/HYDROCHLOROTHIAZIDE	irbesartan-hydrochlorothiazide		
LOSARTAN POTASSIUM	Cozaar		
LOSARTAN POTASSIUM	losartan		
LOSARTAN	Hyzaar		
POTASSIUM/HYDROCHLOROTHIAZIDE			
LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE	losartan-hydrochlorothiazide		
NEBIVOLOL HCL/VALSARTAN	Byvalson		
OLMESARTAN MEDOXOMIL	Benicar		
OLMESARTAN MEDOXOMIL	olmesartan		
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 besylate/valsartan	amlodipine-valsartan		
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid		
candesartan cilexetil	Atacand		
candesartan cilexetil	candesartan		
candesartan cilexetil/hydrochlorothiazide	Atacand HCT		
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid		
irbesartan	irbesartan		
irbesartan/hydrochlorothiazide	irbesartan-hydrochlorothiazide		
losartan potassium	losartan		
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide		
olmesartan medoxomil	Benicar		
	1		

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olmesartan

olmesartan medoxomil



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

Generic Name	Brand Name
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

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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
	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
404.01	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with	Diagnosis	ICD-9-CM
404.03	chronic kidnev disease stage I through stage IV. or unspecified Hypertensive heart and chronic kidney disease, malignant, with heart failure and with	Diagnosis	ICD-9-CM
404.11	chronic kidney disease stage V or end stage renal disease Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic	Diagnosis	ICD-9-CM
404.13	kidney disease stage I through stage IV, or unspecified Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic	Diagnosis	ICD-9-CM
404.91	kidnev disease stage V or end stage renal disease Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with	Diagnosis	ICD-9-CM
404.93	chronic kidney disease stage I through stage IV. or unspecified Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic	Diagnosis	ICD-9-CM
420	kidney disease stage V or end stage renal disease	Diamonia	ICD O CM
428	Heart failure	Diagnosis Diagnosis	ICD-9-CM
428.0 428.1	Congestive heart failure, unspecified Left heart failure	_	ICD-9-CM ICD-9-CM
		Diagnosis	
428.2 428.20	Systolic heart failure	Diagnosis	ICD-9-CM
428.20 428.21	Unspecified systolic heart failure Acute systolic heart failure	Diagnosis	ICD-9-CM ICD-9-CM
428.21	Chronic systolic heart failure	Diagnosis	ICD-9-CM
428.23	Acute on chronic systolic heart failure	Diagnosis Diagnosis	ICD-9-CM
428.3	Diastolic heart failure	Diagnosis	ICD-9-CM
428.30	Unspecified diastolic heart failure	Diagnosis	ICD-9-CM
428.31	Acute diastolic heart failure	Diagnosis	ICD-9-CM
428.31	Chronic diastolic heart failure	Diagnosis	ICD-9-CM
428.33	Acute on chronic diastolic heart failure	Diagnosis	ICD-9-CM
428.33	Combined systolic and diastolic heart failure		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
	Acute on chronic combined systolic and diastolic heart failure	Diagnosis	
428.43 428.9	Unspecified heart failure	Diagnosis	ICD-9-CM ICD-9-CM
	·	Diagnosis	
111.0	Hypertensive heart disease with heart failure	Diagnosis	ICD-10-CM
113.0	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease	_	ICD-10-CM
113.2	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease	Diagnosis	ICD-10-CM
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
150.30	Unspecified diastolic (congestive) heart failure	Diagnosis	ICD-10-CM
150.31	Acute 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
150.32	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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	ever if (nCrC3) codes osed to befine characteristics in this request	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
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

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	ever ii (neres) codes osed to Deline Characteristics iii this Request	Code	
Code	Description	Category	Code Type
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
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

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Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Characteristics in this Request

		Code	
Code	Description	Category	Code Type
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
	Anaphylactic reaction due to unspecified food, initial encounter	Diagnosis	ICD-10-CM
	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		Diagnosis	ICD-10-CM
	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		Diagnosis	ICD-10-CM
	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
T78.02A3	Anaphylactic reaction due to other fish	Diagnosis	ICD-10-CM
T78.03XA		Diagnosis	ICD-10-CIVI
T78.03XA	• •	Diagnosis	ICD-10-CM
T78.03XS	Anaphylactic reaction due to other fish, sequela	Diagnosis	ICD-10-CM
T78.03A3	Anaphylactic reaction due to other rish, sequela Anaphylactic reaction due to fruits and vegetables	Diagnosis	ICD-10-CM
170.04	Thisphylactic reaction due to maits and resetables	Diagnosis	ICD TO-CIVI

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	ever ii (HCPCS) Codes Osed to Define Characteristics in this Request	Code	
Code	Description	Category	Code Type
	Anaphylactic reaction due to fruits and vegetables, initial encounter	Diagnosis	ICD-10-CM
	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
	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
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
	encounter		
T80.51XS	Anaphylactic reaction due to administration of blood and blood products, sequela	Diagnosis	ICD-10-CM
T80.52	Anaphylactic reaction due to vaccination	Diagnosis	ICD-10-CM
T80.52XA		Diagnosis	ICD-10-CM
	Anaphylactic reaction due to vaccination, subsequent encounter	Diagnosis	ICD-10-CM
T80.52XS	Anaphylactic reaction due to vaccination, sequela	Diagnosis	ICD-10-CM
T80.59	Anaphylactic reaction due to other serum	Diagnosis	ICD-10-CM
T80.59XA		Diagnosis	ICD-10-CM
	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 adverse effect of correct drug or medicament properly administered	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
T88.6XXA	Anaphylactic reaction due to adverse effect of correct drug or medicament properly	Diagnosis	ICD-10-CM
	administered, initial encounter	_	
T88.6XXD		Diagnosis	ICD-10-CM
	administered, subsequent encounter		
T88.6XXS	Anaphylactic reaction due to adverse effect of correct drug or medicament properly	Diagnosis	ICD-10-CM
	administered, sequela		
V07.1	Need for desensitization to allergens	Diagnosis	ICD-9-CM
V13.81	Personal history of anaphylaxis	Diagnosis	ICD-9-CM
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
V14.3	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	Diagnosis	ICD-10-CM
Z88.2	Allergy status to sulfonamides	Diagnosis	ICD-10-CM
Z88.3	Allergy status to other anti-infective agents	Diagnosis	ICD-10-CM
Z88.4	Allergy status to anesthetic agent	Diagnosis	ICD-10-CM
Z88.5	Allergy status to narcotic agent	Diagnosis	ICD-10-CM
Z88.6	Allergy status to analgesic agent	Diagnosis	ICD-10-CM
Z88.7	Allergy status to serum and vaccine	Diagnosis	ICD-10-CM
Z88.8	Allergy status to other drugs, medicaments and biological substances	Diagnosis	ICD-10-CM
Z88.9	Allergy status to unspecified drugs, medicaments and biological substances	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

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		Code	
Code	Description	Category	Code Type
	Angioedema		
995.1	Angioneurotic edema not elsewhere classified	Diagnosis	ICD-9-CM
T783XXA	Angioneurotic edema, initial encounter	Diagnosis	ICD-10-CM
T783XXD	Angioneurotic edema, subsequent encounter	Diagnosis	ICD-10-CM
T783XXS	Angioneurotic edema, sequela	Diagnosis	ICD-10-CM
250	Diabetes	<u> </u>	100.0.014
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	Diagnosis	ICD-9-CM
250.01	as uncontrolled Diabetes mellitus without mention of complication, type I [juvenile type], not stated as	Diagnosis	ICD-9-CM
250.02	uncontrolled Diabetes mellitus without mention of complication, type II or unspecified type,	Diagnosis	ICD-9-CM
250.02	uncontrolled	Diagnosis	ICD 5 CIVI
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
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	Diagnosis	ICD-9-CM
250.51	uncontrolled 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
250.52	Diabetes with ophthalmic manifestations, type if of unspectified type, uncontrolled	Diagnosis	ICD-9-CIVI
250.55	Diabetes with neurological manifestations	Diagnosis	ICD-9-CM
250.60	Diabetes with neurological manifestations, type II or unspecified type, not stated as	Diagnosis	ICD-9-CM
	uncontrolled	_	
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

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		Code	
Code	Description	Category	Code Type
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	Diagnosis	ICD-9-CM
250.71	uncontrolled 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	Diagnosis	ICD-9-CM
250.82	uncontrolled Diabetes with other specified manifestations, type II or unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.82	Diabetes with other specified manifestations, type II of unspecified type, uncontrolled	Diagnosis	ICD-9-CM
250.83	Diabetes with unspecified complication	Diagnosis	ICD-9-CM
250.90	Diabetes with unspecified complication, type II or unspecified type, not stated as	Diagnosis	ICD-9-CM
250.50	uncontrolled	Diagnosis	ieb 5 eivi
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
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-	Procedure	HCPCS
	shelf 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 from cast(s) of patient's foot (custom molded shoe), per shoe	Procedure	HCPCS
A5503	For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or	Procedure	HCPCS
A5504	custom molded shoe with roller or rigid rocker bottom, per shoe For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or	Procedure	HCPCS
A5505	custom molded shoe with wedge(s), per shoe For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or	Procedure	HCPCS
A5506	custom molded shoe with metatarsal bar, per shoe For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or	Procedure	HCPCS
A5507	custom molded shoe with off-set heel(s), per shoe For diabetics only, not otherwise specified modification (including fitting) of off-the-shelf	Procedure	HCPCS
	depth-inlay shoe or custom molded shoe, per shoe		
A5508	For diabetics only, deluxe feature of off-the-shelf depth-inlay shoe or custom molded shoe, per shoe	Procedure	HCPCS
A5510	For diabetics only, direct formed, compression molded to patient's foot without external heat source, multiple-density insert(s) prefabricated, per shoe	Procedure	HCPCS
A5512	For diabetics only, multiple density insert, direct formed, molded to foot after external	Procedure	HCPCS
	heat 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 A 35 durometer or 3/16 inch material of Shore A 40 durometer (or higher), prefabricated, each		
A5513	For diabetics only, multiple density insert, custom molded from model of patient's foot,	Procedure	HCPCS
A3313	total 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 shaping material,	riocedure	TICFCS
	custom fabricated, each		
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

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System, Le	ever if (HCPCS) Codes osed to Define Characteristics in this Request	Code	
Code	Description	Category	Code Type
E10.21	Type 1 diabetes mellitus with diabetic nephropathy	Diagnosis	ICD-10-CM
E10.22	Type 1 diabetes mellitus with diabetic chronic kidney disease	Diagnosis	ICD-10-CM
E10.29	Type 1 diabetes mellitus with other diabetic kidney complication	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	Diagnosis	ICD-10-CM
E10.3212	edema, right eve Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3213	edema. left eve Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3219	edema. bilateral Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3291	edema, unspecified eve Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E10.3292	edema. right eve Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E10.3293	edema. left eve Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E10.3299	edema, bilateral Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E10.3311	edema. unspecified eve Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3312	edema. right eve Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3313	edema, left eve Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3319	edema, bilateral Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3391	edema. unspecified eve Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E10.3392	macular edema, right eve Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E10.3393	macular edema, left eve Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E10.3399	macular edema, bilateral Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E10.3411	macular edema. unspecified eve Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3412	edema. right eve Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E10.3413	edema. left eve 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
E10.3491	edema, unspecified eve Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E10.3492	edema, right eye Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye	Diagnosis	ICD-10-CM

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		Code	·
Code	Description	Category	Code Type
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 eve		
E10.3511	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right	Diagnosis	ICD-10-CM
	eve		
E10.3512	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left	Diagnosis	ICD-10-CM
	eve		
E10.3513	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
540 2540	bilateral The Control of the Control	5	100 40 614
E10.3519	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
F10 2F21	unspecified eve	Diagnasis	ICD 10 CM
E10.3521	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
E10.3522	detachment involving the macula, right eve Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
L10.3322	detachment involving the macula, left eve	Diagnosis	ICD-10-CIVI
E10.3523	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment involving the macula, bilateral	2.0800.0	.02 20 0
E10.3529	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment involving the macula, unspecified eve	J	
E10.3531	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment not involving the macula, right eye		
E10.3532	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment not involving the macula, left eve		
E10.3533	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
	detachment not involving the macula, bilateral		
E10.3539	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
E40 2E44	detachment not involving the macula, unspecified eve	Diamaria	100 40 614
E10.3541	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
E10.3542	retinal detachment and rhegmatogenous retinal detachment, right eve Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
L10.3342	retinal detachment and rhegmatogenous retinal detachment, left eye	Diagnosis	ICD-10-CIVI
E10.3543	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
L10.5545	retinal detachment and rhegmatogenous retinal detachment, bilateral	Diagnosis	100 10 011
E10.3549	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
	retinal detachment and rhegmatogenous retinal detachment, unspecified eve	. 0	
E10.3551	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye	Diagnosis	ICD-10-CM
E10.3552	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye	Diagnosis	ICD-10-CM
E10.3553	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	Diagnosis	ICD-10-CM
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,	Diagnosis	ICD-10-CM
	right eve		
E10.3592	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema,	Diagnosis	ICD-10-CM
	left eye		
E10.3593	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema,	Diagnosis	ICD-10-CM
E40 2502	bilateral	Di '	100 40 614
E10.3599	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema,	Diagnosis	ICD-10-CM
E10.26	unspecified eve	Diagnosis	ICD-10-CM
E10.36	Type 1 diabetes mellitus with diabetic cataract	Diagnosis	ICD-TO-CIAI

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		Code	
Code	Description	Category	Code Type
E10.37X1	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, right	Diagnosis	ICD-10-CM
	eve		
E10.37X2	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, left	Diagnosis	ICD-10-CM
	eve		
E10.37X3	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment,	Diagnosis	ICD-10-CM
	bilateral		
E10.37X9	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment,	Diagnosis	ICD-10-CM
	unspecified eve		
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-	Diagnosis	ICD-10-CM
	hvperosmolar coma (NKHHC)		
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
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	Diagnosis	ICD-10-CM
	edema, right eve		
E11.3212	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, left eye		
E11.3213	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, bilateral		
E11.3219	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
	edema, unspecified eve		
E11.3291	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
	edema, right eye		

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		Code	
Code	Description	Category	Code Type
E11.3292	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3293	edema, left eve Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3299	edema. bilateral Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3311	edema, unspecified eve Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3312	edema, right eve Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3313	edema. left eve Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3319	edema, bilateral Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3391	edema, unspecified eve Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E11.3392	macular edema, right eve Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E11.3393	macular edema, left eve Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E11.3399	macular edema. bilateral Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E11.3411	macular edema, unspecified eye Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3412	edema, right eve Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3413	edema. left eve Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3419	edema, bilateral Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E11.3491	edema, unspecified eve Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3492	edema, right eve Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3493	edema. left eve Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3499	edema, bilateral Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular	Diagnosis	ICD-10-CM
E11.3511	edema, unspecified eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right	Diagnosis	ICD-10-CM
E11.3512	eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left	Diagnosis	ICD-10-CM
E11.3513	eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E11.3519	bilateral Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema,	Diagnosis	ICD-10-CM
E11.3521	unspecified eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
E11.3522	detachment involving the macula, right eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye	Diagnosis	ICD-10-CM

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<u> </u>	ever ii (neres) codes osed to beinie characteristics iii this nequest	Code	
Code	Description	Category	Code Type
E11.3523		Diagnosis	ICD-10-CM
E11.3529	detachment involving the macula, bilateral Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
E11.3531	detachment involving the macula, unspecified eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
E11.3532	7	Diagnosis	ICD-10-CM
E11.3533	detachment not involving the macula. left eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
E11.3539	detachment not involving the macula, bilateral Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal	Diagnosis	ICD-10-CM
E11.3541	detachment not involving the macula, unspecified eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
E11.3542	retinal detachment and rhegmatogenous retinal detachment, right eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
E11.3543	retinal detachment and rhegmatogenous retinal detachment, left eve Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
E11.3549	retinal detachment and rhegmatogenous retinal detachment, bilateral Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction	Diagnosis	ICD-10-CM
E11.3551	retinal detachment and rhegmatogenous retinal detachment, unspecified eve Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, right eye	Diagnosis	ICD-10-CM
E11.3551	•	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 eve	Diagnosis	ICD-10-CM
E11.3592		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 eve	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 eve	Diagnosis	ICD-10-CM
E11.37X2	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, left eve	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 eve	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

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	Code	
Description	Category	Code Type
Type 2 diabetes mellitus with other circulatory complications	Diagnosis	ICD-10-CM
Type 2 diabetes mellitus with diabetic neuropathic arthropathy	Diagnosis	ICD-10-CM
Type 2 diabetes mellitus with other diabetic arthropathy	Diagnosis	ICD-10-CM
Type 2 diabetes mellitus with diabetic dermatitis	Diagnosis	ICD-10-CM
Type 2 diabetes mellitus with foot ulcer	Diagnosis	ICD-10-CM
Type 2 diabetes mellitus with other skin ulcer	Diagnosis	ICD-10-CM
Type 2 diabetes mellitus with other skin complications	Diagnosis	ICD-10-CM
Type 2 diabetes mellitus with periodontal disease	Diagnosis	ICD-10-CM
	_	ICD-10-CM
	Diagnosis	ICD-10-CM
	Diagnosis	ICD-10-CM
	_	ICD-10-CM
	Diagnosis	ICD-10-CM
	Diagnosis	ICD 10 CM
		ICD-10-CM
•	_	ICD-10-CM ICD-10-CM
·	_	ICD-10-CM
	_	ICD-10-CM
·	_	ICD-10-CW
		ICD-10-CW
	Diagnosis	ICD-10-CIVI
Other specified diabetes mellitus with unspecified diabetic retinopathy without macular	Diagnosis	ICD-10-CM
Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
	Diagnosis	ICD-10-CM
macular edema, left eve	.0	
	Diagnosis	ICD-10-CM
	Diagnosis	ICD-10-CM
macular edema, unspecified eve		
	Diagnosis	ICD-10-CM
Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
macular edema. left eve Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
macular edema, bilateral	5	100 40 604
	Diagnosis	ICD-10-CM
$Other\ specified\ diabetes\ mellitus\ with\ moderate\ nonproliferative\ diabetic\ retinopathy\ with$	Diagnosis	ICD-10-CM
	Diagnosis	ICD-10-CM
macular edema, left eye	_	.02 20 0111
Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral	Diagnosis	ICD-10-CM
	Type 2 diabetes mellitus with other circulatory complications Type 2 diabetes mellitus with diabetic neuropathic arthropathy Type 2 diabetes mellitus with diabetic dermatitis Type 2 diabetes mellitus with diabetic dermatitis Type 2 diabetes mellitus with diabetic dermatitis Type 2 diabetes mellitus with other skin ulcer Type 2 diabetes mellitus with other skin ulcer Type 2 diabetes mellitus with other skin complications Type 2 diabetes mellitus with other aco complications Type 2 diabetes mellitus with other aco complications Type 2 diabetes mellitus with there or a complications Type 2 diabetes mellitus with there or a complications Type 2 diabetes mellitus with thypoglycemia with coma Type 2 diabetes mellitus with thyperglycemia Type 2 diabetes mellitus with other specified complication Type 2 diabetes mellitus with other specified complication Type 2 diabetes mellitus with other specified complications Other specified diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar come (NKHHC) Other specified diabetes mellitus with hyperosmolarity with coma Other specified diabetes mellitus with diabetic neophropathy Other specified diabetes mellitus with diabetic chronic kidney disease Other specified diabetes mellitus with diabetic chronic kidney complication Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema. Ieft eve Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema. Jeft eve Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema. Ieft eve Other specified diabetes mellitus with mil	Type 2 diabetes mellitus with other circulatory complications Type 2 diabetes mellitus with diabetic neuropathic arthropathy Diagnosis Type 2 diabetes mellitus with other diabetic arthropathy Diagnosis Type 2 diabetes mellitus with diabetic dermatitis Type 2 diabetes mellitus with foot ulcer Diagnosis Type 2 diabetes mellitus with other skin ulcer Diagnosis Type 2 diabetes mellitus with other skin complications Diagnosis Type 2 diabetes mellitus with other skin complications Diagnosis Type 2 diabetes mellitus with other oral complications Diagnosis Type 2 diabetes mellitus with other oral complications Diagnosis Type 2 diabetes mellitus with other oral complications Diagnosis Type 2 diabetes mellitus with hypoglycemia without coma Diagnosis Type 2 diabetes mellitus with hypoglycemia without coma Diagnosis Type 2 diabetes mellitus with other specified complication Diagnosis Type 2 diabetes mellitus with other specified complications Diagnosis Type 2 diabetes mellitus with unspecified complications Diagnosis Diag

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2,000,000	ever if (HCPCS) Codes Osed to Define Characteristics in this Request	Code	
Code	Description	Category	Code Type
E13.3319	$Other\ specified\ diabetes\ mellitus\ with\ moderate\ nonproliferative\ diabetic\ retinopathy\ with$	Diagnosis	ICD-10-CM
E13.3391	macular edema, unspecified eve Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy	Diagnosis	ICD-10-CM
E13.3392	without macular edema, right eve Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy	Diagnosis	ICD-10-CM
E13.3393	without macular edema, left eve Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral	Diagnosis	ICD-10-CM
E13.3399	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eve	Diagnosis	ICD-10-CM
E13.3411	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eve	Diagnosis	ICD-10-CM
E13.3412	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
E13.3413	macular edema, left eve Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
E13.3419	macular edema, bilateral Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with	Diagnosis	ICD-10-CM
E13.3491	macular edema, unspecified eve Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E13.3492	macular edema, right eve Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E13.3493	macular edema, left eye Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E13.3499	macular edema. bilateral Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without	Diagnosis	ICD-10-CM
E13.3511	macular edema, unspecified eve Other specified diabetes mellitus with proliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E13.3512	edema, right eve Other specified diabetes mellitus with proliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E13.3513	edema. left eve Other specified diabetes mellitus with proliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E13.3519	edema, bilateral Other specified diabetes mellitus with proliferative diabetic retinopathy with macular	Diagnosis	ICD-10-CM
E13.3521	edema, unspecified eve Other specified diabetes mellitus with proliferative diabetic retinopathy with traction	Diagnosis	ICD-10-CM
E13.3522	retinal detachment involving the macula, right eve Other specified diabetes mellitus with proliferative diabetic retinopathy with traction	Diagnosis	ICD-10-CM
E13.3523	retinal detachment involving the macula, left eve Other specified diabetes mellitus with proliferative diabetic retinopathy with traction	Diagnosis	ICD-10-CM
E13.3529	retinal detachment involving the macula, bilateral Other specified diabetes mellitus with proliferative diabetic retinopathy with traction	Diagnosis	ICD-10-CM
E13.3531	retinal detachment involving the macula, unspecified eve Other specified diabetes mellitus with proliferative diabetic retinopathy with traction	Diagnosis	ICD-10-CM
E13.3532	retinal detachment not involving the macula, right eye Other specified diabetes mellitus with proliferative diabetic retinopathy with traction	Diagnosis	ICD-10-CM
E13.3533	retinal detachment not involving the macula, left eve Other specified diabetes mellitus with proliferative diabetic retinopathy with traction	Diagnosis	ICD-10 CM
£13.3333	retinal detachment not involving the macula, bilateral	Diagnosis	ICD-10-CM
E13.3539	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye	Diagnosis	ICD-10-CM

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		Code	_
Code	Description	Category	Code Type
E13.3541	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined	Diagnosis	ICD-10-CM
	traction retinal detachment and rhegmatogenous retinal detachment, right eye		
E13.3542	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye	Diagnosis	ICD-10-CM
E13.3543	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral	Diagnosis	ICD-10-CM
E13.3549	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye	Diagnosis	ICD-10-CM
E13.3551	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, right eye	Diagnosis	ICD-10-CM
E13.3552	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, left eye	Diagnosis	ICD-10-CM
E13.3553	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	Diagnosis	ICD-10-CM
E13.3559	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eve	Diagnosis	ICD-10-CM
E13.3591	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye	Diagnosis	ICD-10-CM
E13.3592	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eve	Diagnosis	ICD-10-CM
E13.3593	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral	Diagnosis	ICD-10-CM
E13.3599	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eve	Diagnosis	ICD-10-CM
E13.36	Other specified diabetes mellitus with diabetic cataract	Diagnosis	ICD-10-CM
E13.37X1	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, right eve	Diagnosis	ICD-10-CM
E13.37X2	Other specified diabetes mellitus with diabetic macular edema, resolved following	Diagnosis	ICD-10-CM
E13.37X3	treatment. left eve Other specified diabetes mellitus with diabetic macular edema, resolved following	Diagnosis	ICD-10-CM
E13.37X9	treatment, bilateral Other specified diabetes mellitus with diabetic macular edema, resolved following	Diagnosis	ICD-10-CM
E13.39	treatment, unspecified eve Other specified diabetes mellitus with other diabetic ophthalmic complication	Diagnosis	ICD-10-CM
E13.40	Other specified diabetes mellitus with diabetic neuropathy, unspecified	Diagnosis	ICD-10-CM
E13.41	Other specified diabetes mellitus with diabetic mononeuropathy	Diagnosis	ICD-10-CM
E13.42	Other specified diabetes mellitus with diabetic polyneuropathy	Diagnosis	ICD-10-CM
E13.43	Other specified diabetes mellitus with diabetic autonomic (poly)neuropathy	Diagnosis	ICD-10-CM
E13.44	Other specified diabetes mellitus with diabetic amyotrophy	Diagnosis	ICD-10-CM
E13.49	Other specified diabetes mellitus with other diabetic neurological complication	Diagnosis	ICD-10-CM
E13.51	Other specified diabetes mellitus with diabetic peripheral angiopathy without gangrene	Diagnosis	ICD-10-CM
E13.52	Other specified diabetes mellitus with diabetic peripheral angiopathy with gangrene	Diagnosis	ICD-10-CM
E13.59	Other specified diabetes mellitus with other circulatory complications	Diagnosis	ICD-10-CM
E13.610	Other specified diabetes mellitus with diabetic neuropathic arthropathy	Diagnosis	ICD-10-CM
E13.618	Other specified diabetes mellitus with other diabetic arthropathy	Diagnosis	ICD-10-CM

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System, E	ever if (fici cs) codes osed to befine characteristics in this nequest		
		Code	
Code	Description	Category	Code Type
E13.620	Other specified diabetes mellitus with diabetic dermatitis	Diagnosis	ICD-10-CM
E13.621	Other specified diabetes mellitus with foot ulcer	Diagnosis	ICD-10-CM
E13.622	Other specified diabetes mellitus with other skin ulcer	Diagnosis	ICD-10-CM
E13.628	Other specified diabetes mellitus with other skin complications	Diagnosis	ICD-10-CM
E13.630	Other specified diabetes mellitus with periodontal disease	Diagnosis	ICD-10-CM
E13.638	Other specified diabetes mellitus with other oral complications	Diagnosis	ICD-10-CM
E13.641	Other specified diabetes mellitus with hypoglycemia with coma	Diagnosis	ICD-10-CM
E13.649	Other specified diabetes mellitus with hypoglycemia without coma	Diagnosis	ICD-10-CM
E13.65	Other specified diabetes mellitus with hyperglycemia	Diagnosis	ICD-10-CM
E13.69	Other specified diabetes mellitus with other specified complication	Diagnosis	ICD-10-CM
E13.8 E13.9	Other specified diabetes mellitus with unspecified complications	Diagnosis	ICD-10-CM
G0108	Other specified diabetes mellitus without complications Diabetes outpatient self management training services, individual, per 20 minutes	Diagnosis Procedure	ICD-10-CM HCPCS
	Diabetes outpatient self-management training services, individual, per 30 minutes	Procedure	HCPCS
G0109	Diabetes outpatient self-management training services, group session (two or more), per 30 minutes	Procedure	псрсз
G0245	Initial physician evaluation and management of a diabetic patient with diabetic sensory neuropathy resulting in a loss of protective sensation (LOPS) which must include: (1) the	Procedure	HCPCS
	diagnosis of LOPS, (2) a patient history, (3) a physical examination that consists of at least		
	the following elements: (a) visual inspection of the forefoot, hindfoot, and toe web spaces,		
	(b) evaluation of a protective sensation, (c) evaluation of foot structure and biomechanics,		
	(d) evaluation of vascular status and skin integrity, and (e) evaluation and recommendation		
	of footwear, and (4) patient education		
G0246	Follow-up physician evaluation and management of a diabetic patient with diabetic	Procedure	HCPCS
	sensory neuropathy resulting in a loss of protective sensation (LOPS) to include at least the		
	following: (1) a patient history, (2) a physical examination that includes: (a) visual		
	inspection of the forefoot, hindfoot, and toe web spaces, (b) evaluation of protective		
	sensation, (c) evaluation of foot structure and biomechanics, (d) evaluation of vascular		
	status and skin integrity, and (e) evaluation and recommendation of footwear, and (3)		
	patient education		
G0247	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 the following, if present: (1) local		
	care of superficial wounds, (2) debridement of corns and calluses, and (3) trimming and		
	debridement of nails		
G8015	Diabetic patient with most recent hemoglobin A1c level (within the last 6 months)	Procedure	HCPCS
	documented as greater than 9%		
G8016	Diabetic patient with most recent hemoglobin A1c level (within the last 6 months)	Procedure	HCPCS
	documented as less than or equal to 9%		
G8017	Clinician documented that diabetic patient was not eligible candidate for hemoglobin A1c	Procedure	HCPCS
	measure		
G8018	Clinician has not provided care for the diabetic patient for the required time for	Procedure	HCPCS
00040	hemoglobin A1c measure (6 months)		
G8019	Diabetic patient with most recent low-density lipoprotein (within the last 12 months)	Procedure	HCPCS
00000	documented as greater than or equal to 100 mg/dl		
G8020	Diabetic patient with most recent low-density lipoprotein (within the last 12 months)	Procedure	HCPCS
C0034	documented as less than 100 mg/dl	Dun ne di	HCDCC
G8021	Clinician documented that diabetic patient was not eligible candidate for low-density	Procedure	HCPCS
	lipoprotein measure		

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		Code	
Code	Description Clinician has not provided care for the diabetic patient for the required time for low-	Category	Code Type
G8022	·	Procedure	HCPCS
G8023	density lipoprotein measure (12 months) Diabetic patient with most recent blood pressure (within the last 6 months) documented	Procedure	HCPCS
00023	as equal to or greater than 140 systolic or equal to or greater than 80 mm Hg diastolic	rroccaure	Tier es
	as equal to of greater than 140 systolic of equal to of greater than 50 min rig diastolic		
G8024	Diabetic patient with most recent blood pressure (within the last 6 months) documented	Procedure	HCPCS
	as less than 140 systolic and less than 80 diastolic		
G8025	Clinician documented that the diabetic patient was not eligible candidate for blood	Procedure	HCPCS
	pressure measure		
G8026	Clinician has not provided care for the diabetic patient for the required time for blood	Procedure	HCPCS
	pressure measure (within the last 6 months)		
G8332	Clinician has not provided care for the diabetic retinopathy patient for the required time	Procedure	HCPCS
60222	for macular edema and retinopathy measurement		Hence
G8333	Patient documented to have had findings of macular or fundus exam communicated to the	Procedure	HCPCS
G8334	physician managing the diabetes care Documentation of findings of macular or fundus exam not communicated to the physician	Procedure	HCPCS
00334		Procedure	псесз
	managing the patient's ongoing diabetes care		
G8335	Clinician documentation that patient was not an eligible candidate for the findings of their	Procedure	HCPCS
	macular or fundus exam being communicated to the physician managing their diabetes		
	care during the reporting year		
G8336	Clinician has not provided care for the diabetic retinopathy patient for the required time	Procedure	HCPCS
00330	for physician communication measurement	rroccaare	1101 05
G8385	Diabetic patients with no documentation of hemoglobin A1c level (within the last 12	Procedure	HCPCS
	months)		
G8386	Diabetic patients with no documentation of low-density lipoprotein (within the last 12	Procedure	HCPCS
	months)		
G8390	Diabetic patients with no documentation of blood pressure measurement (within the last	Procedure	HCPCS
	12 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
414.01 414.02	Coronary atherosclerosis of native coronary artery Coronary atherosclerosis of autologous vein bypass graft	Diagnosis	ICD-9-CM
414.02	Coronary atheroscierosis of autologous vein bypass graft Coronary atherosclerosis of nonautologous biological bypass graft	Diagnosis Diagnosis	ICD-9-CM 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
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		Code	·
Code	Description	Category	Code Type
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 calcified coronary lesion	Diagnosis	ICD-9-CM
414.8	Other specified forms of chronic ischemic heart disease	Diagnosis	ICD-9-CM
414.9	Unspecified chronic ischemic heart disease	Diagnosis	ICD-9-CM
429.2	Unspecified cardiovascular disease	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	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-	Procedure	HCPCS
	blocker therapy		
G8034	Prior myocardial infarction, coronary artery disease patient not documented to be on beta-	Procedure	HCPCS
	blocker therapy		
G8035	Clinician documented that prior myocardial infarction, coronary artery disease patient was	Procedure	HCPCS
00000	not eligible candidate for beta-blocker therapy measure		
G8036	Coronary artery disease patient documented to be on antiplatelet therapy	Procedure	HCPCS
G8037	Coronary artery disease patient not documented to be on antiplatelet therapy	Procedure	HCPCS
G8038	Clinician documented that coronary artery disease patient was not eligible candidate for	Procedure	HCPCS
C9020	antiplatelet therapy measure	Dracadura	HCDCC
G8039	Coronary artery disease patient with low-density lipoprotein documented to be greater	Procedure	HCPCS
G8040	than 100 mg/dl Coronary artery disease patient with low-density lipoprotein documented to be less than	Procedure	HCPCS
G6040	or equal to 100 mg/dl	Procedure	псесз
G8041	Clinician documented that coronary artery disease patient was not eligible candidate for	Procedure	HCPCS
00041	low-density lipoprotein measure	riocedare	rici cs
120.0	Unstable angina	Diagnosis	ICD-10-CM
120.0	Angina pectoris with documented spasm	Diagnosis	ICD-10-CM
120.1	Other forms of angina pectoris	Diagnosis	ICD-10-CM
120.8	Angina pectoris, unspecified	Diagnosis	ICD-10-CM
123.0	Hemopericardium as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.0	Atrial septal defect as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.1	Ventricular septal defect as current complication following acute myocardial infarction	Diagnosis	ICD-10-CM
123.2	ventricular septar defect as current complication following acute myocardia infarction	Diagnosis	ICD-10-CIVI
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	Diagnosis	ICD-10-CM
	infarction		
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	Diagnosis	ICD-10-CM
	following acute myocardial infarction		

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		Code	
Code	Description	Category	Code Type
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	Diagnosis	ICD-10-CM
	documented spasm		
125.118	Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris	Diagnosis	ICD-10-CM
I25.119	Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris	Diagnosis	ICD-10-CM
125.3	Aneurysm of heart	Diagnosis	ICD-10-CM
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	Diagnosis	ICD-10-CM
125.701	pectoris Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with	Diagnosis	ICD-10-CM
125.708	documented spasm Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina	Diagnosis	ICD-10-CM
125.709	pectoris Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina	Diagnosis	ICD-10-CM
125.710	pectoris 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	Diagnosis	ICD-10-CM
125.718	with documented spasm Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of	Diagnosis	ICD-10-CM
125.719	angina pectoris Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina	Diagnosis	ICD-10-CM
125.720	pectoris Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina	Diagnosis	ICD-10-CM
125.721	pectoris Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris	Diagnosis	ICD-10-CM
125.728	with documented spasm Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of	Diagnosis	ICD-10-CM
125.729	angina pectoris Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified	Diagnosis	ICD-10-CM
125.730	angina pectoris 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	Diagnosis	ICD-10-CM
125.738	pectoris with documented spasm Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris	Diagnosis	ICD-10-CM

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		Code	
Code	Description	Category	Code Type
125.739	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with	Diagnosis	ICD-10-CM
	unspecified angina pectoris		
125.750	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	Diagnosis	ICD-10-CM
125.758	documented spasm Atherosclerosis of native coronary artery of transplanted heart with other forms of angina	Diagnosis	ICD-10-CM
125.756		Diagnosis	ICD-10-CIVI
125.759	Atherosclerosis of native coronary artery of transplanted heart with unspecified angina	Diagnosis	ICD-10-CM
125.760	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable	Diagnosis	ICD-10-CM
125.761	angina Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina	Diagnosis	ICD-10-CM
	pectoris with documented spasm		
125.768	Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris	Diagnosis	ICD-10-CM
125.769	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified	Diagnosis	ICD-10-CM
125 700	angina pectoris	Diagram :	ICD 40 Ct 4
125.790 125.791	Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with	Diagnosis Diagnosis	ICD-10-CM ICD-10-CM
125.791	documented spasm	Diagnosis	ICD-10-CIVI
125.798	Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris	Diagnosis	ICD-10-CM
125.799	Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris	Diagnosis	ICD-10-CM
125.810	Atherosclerosis of coronary artery bypass graft(s) without angina pectoris	Diagnosis	ICD-10-CM
125.811	Atherosclerosis of native coronary artery of transplanted heart without angina pectoris	Diagnosis	ICD-10-CM
125.812	Atherosclerosis of bypass graft of coronary artery of transplanted heart without angina pectoris	Diagnosis	ICD-10-CM
125.82	Chronic total occlusion of coronary artery	Diagnosis	ICD-10-CM
125.83	Coronary atherosclerosis due to lipid rich plaque	Diagnosis	ICD-10-CM
125.84	Coronary atherosclerosis due to calcified coronary lesion	Diagnosis	ICD-10-CM
125.89	Other forms of chronic ischemic heart disease	Diagnosis	ICD-10-CM
125.9	Chronic ischemic heart disease, unspecified	Diagnosis	ICD-10-CM
151.0	Cardiac septal defect, acquired	Diagnosis	ICD-10-CM
151.1	Rupture of chordae tendineae, not elsewhere classified	Diagnosis	ICD-10-CM
151.2	Rupture of papillary muscle, not elsewhere classified	Diagnosis	ICD-10-CM
151.9	Heart disease, unspecified	Diagnosis	ICD-10-CM
152	Other heart disorders in diseases classified elsewhere	Diagnosis	ICD-10-CM
F04	Renal Disorders	Diamania	ICD 0 CM
584	Acute kidney failure	Diagnosis	ICD-9-CM
584.5	Acute kidney failure with lesion of tubular necrosis	Diagnosis	ICD-9-CM
584.6 584.7	Acute kidney failure with lesion of renal cortical necrosis Acute kidney failure with lesion of medullary [papillary] necrosis	Diagnosis Diagnosis	ICD-9-CM ICD-9-CM
584.7 584.8	Acute kidney failure with lesion of meduliary [papiliary] necrosis 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 (CKD) 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
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		Code	
Code	Description	Category	Code Type
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
587	Unspecified renal sclerosis	Diagnosis	ICD-9-CM
N17.0	Acute kidney failure with tubular necrosis	Diagnosis	ICD-10-CM
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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Generic Name Brand Name

Allergy Treatments

Cotabflu

Dicopanol

ProAir HFA

Tudorza Pressair

ProAir RespiClick

albuterol sulfate

aldosterone (bulk) aminophylline

aminophylline (bulk)

Proventil HFA

Ventolin HFA

Vospire ER

Lastacaft

Brovana

Astelin

Astepro

Optivar

Dymista

Ticalast

QNASL

Bepreve

Beta-1

Qvar

azelastine

Beconase AQ

Qvar RediHaler Fasenra

Betaloan SUIK

Pod-Care 100CG

Celestone Soluspan

ReadySharp Betamethasone

betamethasone acet, sod phos

betamethasone ace, sodphos-wtr

betamethasone sodphosph-water

betameth ac, sodphos(PF)-water

Child Cough and Sore Throat

Chlorpheniramine Maleate/Codeine

Phosphate/Acetaminophen

DIPHENHYDRAMINE HCL

acetaminophen/dextromethorphan HBr

aclidinium bromide

albuterol sulfate

albuterol sulfate albuterol sulfate

albuterol sulfate

albuterol sulfate

albuterol sulfate

alcaftadine

aldosterone aminophylline

aminophylline

arformoterol tartrate

azelastine HCl azelastine HCl

azelastine HCl azelastine HCl

azelastine HCI/fluticasone propionate

azelastine/fluticasone/sodium chloride/sodium

bicarbonate

beclomethasone dipropionate beclomethasone dipropionate beclomethasone dipropionate

beclomethasone dipropionate

benralizumab bepotastine besilate

betamethasone acetate and sodium phos in sterile

water/PF

betamethasone acetate and sodium

phosph/norflurane/HFC 245fa

betamethasone acetate and sodium

phosph/norflurane/HFC 245fa

betamethasone acetate/betamethasone sodium

phosphate

betamethasone acetate/betamethasone sodium

phosphate

Pod-Care 100C betamethasone acetate/betamethasone sodium

phosphate

betamethasone acetate/betamethasone sodium

phosphate

betamethasone acetate/betamethasone sodium

phosphate

betamethasone acetate/betamethasone sodium

phosphate/water

betamethasone sodium phosph in sterile water for

iniection

brompheniramine maleate J-TAN PD

brompheniramine maleate brompheniramine maleate(bulk)

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Generic Name	Brand Name
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	
brompheniramine maleate/phenylephrine	M-END PE
HCl/codeine phosphate brompheniramine maleate/phenylephrine	Poly-Tussin AC
HCI/codeine phosphate brompheniramine maleate/phenylephrine	AP-Hist DM
HCl/dextromethorphan brompheniramine maleate/phenylephrine	Ala-Hist DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine HCl/dextromethorphan	Altipres-B
brompheniramine maleate/phenylephrine	Bio T Pres-B
HCl/dextromethorphan brompheniramine maleate/phenylephrine	BroveX PEB DM
HCl/dextromethorphan brompheniramine maleate/phenylephrine	Children's Cold and Cough(PE)
HCl/dextromethorphan brompheniramine maleate/phenylephrine	Children's Cold and CoughDM
HCl/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
HCl/dextromethorphan brompheniramine maleate/phenylephrine	Dimaphen DM
HCl/dextromethorphan brompheniramine maleate/phenylephrine	Dimetapp DM Cold-Cough(PE)
HCI/dextromethorphan brompheniramine maleate/phenylephrine	EndaCof - DM
HCI/dextromethorphan	
brompheniramine maleate/phenylephrine HCl/dextromethorphan	Glenmax PEB DM
brompheniramine maleate/phenylephrine HCl/dextromethorphan	Glenmax PEB DM Forte
brompheniramine maleate/phenylephrine	LoHist PEB DM
HCl/dextromethorphan brompheniramine maleate/phenylephrine	LoHist-DM
HCl/dextromethorphan brompheniramine maleate/phenylephrine	M-Hist DM
HCI/dextromethorphan brompheniramine maleate/phenylephrine	Niva-Hist DM
HCl/dextromethorphan brompheniramine maleate/phenylephrine	Presgen B
HCI/dextromethorphan	-
brompheniramine maleate/phenylephrine HCI/dextromethorphan	RelCof DM

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Generic Name	Brand Name
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	
brompheniramine maleate/pseudoephedrine	Atuss DA
HCI/chlophedianol	
brompheniramine maleate/pseudoephedrine	brompheniramine-pseudoeph-DM
HCI/dextromethorphan	
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) Children's Aller-Tec
cetirizine HCl cetirizine HCl	
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 Zyrtec Allergy
cetirizine HCl	Wal-Zyr (cetirizine)
cetirizine HCl	Zyrtec
cetirizine HCl	cetirizine
cetirizine HCI/pseudoephedrine HCI	All Day Allergy-D
cetirizine HCl/pseudoephedrine HCl	Aller-Tec D
cetirizine HCl/pseudoephedrine HCl	Allergy Complete-D
cetirizine HCl/pseudoephedrine HCl	Allergy D-12
cetirizine HCl/pseudoephedrine HCl	Allergy Relief-D (cetirizine)
cetirizine HCl/pseudoephedrine HCl	Allergy-Congest Relief-D (cet)
cetirizine HCl/pseudoephedrine HCl	Cetiri-D
cetirizine HCl/pseudoephedrine HCl	Wal-Zyr D
cetirizine HCI/pseudoephedrine HCI	Zyrtec-D
cetirizine HCl/pseudoephedrine HCl	cetirizine-pseudoephedrine
chlophedianol HCl/guaifenesin	Chlo Tuss EX
chlophedianol HCl/guaifenesin	Vanacof G

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Generic Name	Brand Name
hlophedianol HCl/guaifenesin	chlophedianol-guaifenesin
hlorcyclizine HCl	Ahist (chlorcyclizine)
hlorcyclizine HCI/codeine phosphate	Poly-Tussin
hlorcyclizine HCl/phenylephrine HCl	Dallergy (chlorcyclizine-PE)
hlorcyclizine HCl/pseudoephedrine HCl	Nasopen
hlorcyclizine HCI/pseudoephedrine HCI	Stahist AD
hlorcyclizine HCl/pseudoephedrine	Biclora-D
ICI/chlophedianol HCI	
hlorcyclizine HCl/pseudoephedrine HCl/codeine	Poly-Tussin D
hosphate	,
hlorcyclizine hydrochloride/chlophedianol	Biclora
vdrochloride	
hlorpheniram/phenyleph/dextromethorphn	Cold-Flu M-SymptomDay-Night
acetaminophen/guaifn	
hlorpheniram/phenyleph/dextromethorphn	Tylenol Cold-Flu SevereDay-Nt
acetaminophen/guaifn	Tylenor colu i la octorebaj i te
hlorpheniramine maleate	Aller-Chlor
hlorpheniramine maleate	Allergy (chlorpheniramine)
hlorpheniramine maleate	Allergy 4-Hour
hlorpheniramine maleate	Allergy Relief(chlorpheniramn)
hlorpheniramine maleate	Allergy-Time
hlorpheniramine maleate	Chlor-Trimeton
hlorpheniramine maleate	Chlorphen SR
hlorpheniramine maleate	ED Chlorped Jr
hlorpheniramine maleate	Ed-ChlorPed
hlorpheniramine maleate	Ed-Chlortan
hlorpheniramine maleate	Pharbechlor
hlorpheniramine maleate	Wal-Finate
hlorpheniramine maleate	chlorpheniramine maleate
hlorpheniramine maleate/codeine phosphate	Codar AR
hlorpheniramine maleate/codeine phosphate	EndaCof-C
hlorpheniramine maleate/codeine phosphate	Tuxarin ER
hlorpheniramine maleate/codeine phosphate	Z-Tuss AC
hlorpheniramine maleate/codeine phosphate	Zodryl AC 25
hlorpheniramine maleate/codeine phosphate	Zodryl AC 30
hlorpheniramine maleate/codeine phosphate	Zodryl AC 35
hlorpheniramine maleate/codeine phosphate	Zodryl AC 40
hlorpheniramine maleate/codeine phosphate	Zodryl AC 50
hlorpheniramine maleate/codeine phosphate	Zodryl AC 60
hlorpheniramine maleate/codeine phosphate	Zodryl AC 80
hlorpheniramine maleate/dextromethorphan HBr	Chld Robitussin Night CoughDM
hlorpheniramine maleate/dextromethorphan HBr	Cough and Cold(chlorphen-DM)
hlorpheniramine maleate/dextromethorphan HBr	Cough-Cold Relief HBP
hlorpheniramine maleate/dextromethorphan HBr	Maxi-TussDM(chlorpheniramine)
hlorpheniramine maleate/dextromethorphan HBr	Scot-Tussin DM
hlorpheniramine maleate/phenylephrine HCl	Cold and Allergy
hlorpheniramine maleate/phenylephrine HCl	Sinus and Allergy PE
hlorpheniramine maleate/phenylephrine HCl	Sinus-Allergy (phenylephrine)
hlorpheniramine maleate/phenylephrine	Carbaphen CH
ICI/chlophedianol HCl	err e
hlorpheniramine maleate/phenylephrine	Carbaphen Ped CH

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Generic Name	Brand Name
chlorpheniramine maleate/phenylephrine	ExaPhen CH
HCI/chlophedianol HCl	
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	Cald Dallaf Diva
chlorpheniramine maleate/phenylephrine	Cold Relief Plus
bitartrate/aspirin chlorpheniramine maleate/pseudoephedrine	Tricode AR
HCl/codeine	THEOde An
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 25
HCI/codeine	Zouryr DAC 23
chlorpheniramine maleate/pseudoephedrine	Zodryl DAC 30
HCI/codeine	2001 71 2710 30
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
HCl/ibuprofen	Alvana
ciclesonide	Alvesco
ciclesonide ciclesonide	Omnaris 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 HCl (bulk)
codeine phosphate/guaifenesin	G Tussin AC
codeine phosphate/guaifenesin	Robafen AC
codeine phosphate/guaifenesin	Virtussin AC
codeine phosphate/guaifenesin	codeine-guaifenesin
codeine phosphate/pyrilamine maleate	Pro-Clear AC
codeine polistirex/chlorpheniramine polistirex	Tuzistra XR

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Generic Name	Brand Name
cortisone acetate	cortisone
cromolyn sodium	Nasal Allergy SymptomControl
cromolyn sodium	cromolyn
cyproheptadine HCl	cyproheptadine
cyproheptadine HCl	cyproheptadine (bulk)
deflazacort	Emflaza
desloratadine	Clarinex
desloratadine	desloratadine
desloratadine/pseudoephedrine sulfate	Clarinex-D 12 HOUR
desloratadine/pseudoephedrine sulfate	Clarinex-D 24 HOUR
desoxycorticosterone acetate	desoxycorticosterone ac(bulk)
dexamethasone	Decadron
dexamethasone	DexPak 10 day
dexamethasone	DexPak 13 Day
dexamethasone	DexPak 6 Day
dexamethasone	Dexamethasone Intensol
dexamethasone	Dxevo
dexamethasone	HiDex
dexamethasone	LoCort
dexamethasone	TaperDex
dexamethasone	ZoDex
dexamethasone	ZonaCort
dexamethasone	dexamethasone
dexamethasone acetate and sodium phosphate in	dexamethasone ac, sodph-water
sterile water	l u Note
dexamethasone acetate in sodium chloride,	dexamethas on eace-NaCl, iso-osm
iso-osmotic	development because a majore (b. 111)
dexamethasone acetate, micronized	dexamethasone ac, micro(bulk) Dexonto
dexamethasone sodium phosphate	dexamethasone sod phos(bulk)
dexamethasone sodium phosphate dexamethasone sodium phosphate in 0.9 %	dexamethasone-0.9 % sod.chlor
	dexamethasone-0.5 % sou.cmoi
sodium chloride dexamethasone sodium phosphate/PF	Active Injection Kit D (PF)
dexamethasone sodium phosphate/PF	DoubleDex (PF)
dexamethasone sodium phosphate/PF	MAS Care-Pak (PF)
dexamethasone sodium phosphate/PF	dexamethasone sodium phos(PF)
dexamethasone sodium phosphate/lidocaine HCl	Lidocidex-I
dexamethasone, micronized	dexamethasone,micronized(bulk)
dexamethasone/PF/norflurane/pentafluoropropane	DMT SUIK
(HFC 245fa)	
dexbromphen-pseudoephedrine	M-End DMX
-dextromethorphan	
dexbrompheniramine maleate	Ala-Hist IR
dexbrompheniramine maleate	Pediavent
dexbrompheniramine maleate/chlophedianol HCl	Chlo Hist
dexbrompheniramine maleate/phenylephrine HCl	Ala-Hist PE
dexbrompheniramine maleate/phenylephrine HCl	Dallergy(dexbrompheniramn-PE)
dexbrompheniramine maleate/phenylephrine HCl	dexbrompheniramine-phenyleph
dexbrompheniramine maleate/pseudoephedrine	Acticon (dexbromph-pse)
HCl	NA Ford NATURE
dexbrompheniramine maleate/pseudoephedrine	M-End Max D
HCI/codeine phos	

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Generic Name	Brand Name
dexchlorpheniramine maleate	Ryclora
dexchlorpheniramine maleate	dexchlorpheniramine maleate
dexchlorpheniramine maleate/phenylephrine HCl	Rymed(dexchlorpheniramine-PE)
dexchlorpheniramine maleate/phenylephrine HCl	Stahist (dexchlorpheniramine)
dexchlorpheniramine maleate/phenylephrine	Pro-Red AC (w/dexchlorphenir)
HCI/codeine	Deluturaria DNA
dexchlorpheniramine maleate/phenylephrine/dextromethorphan	Polytussin DM
dextromethorphan	Child Plus Cough and Runny Nose
HBr/acetaminophen/chlorpheniramine maleate dextromethorphan	Child's TylenolplusCough,RNos
HBr/acetaminophen/chlorpheniramine maleate dextromethorphan	Coricidin HBP Flu
HBr/acetaminophen/chlorpheniramine maleate dextromethorphan	Flu BP
HBr/acetaminophen/chlorpheniramine maleate	51, 1100
dextromethorphan HBr/acetaminophen/chlorpheniramine maleate	Flu HBP
dextromethorphan HBr/acetaminophen/chlorpheniramine maleate	Maximum Strength Flu
dextromethorphan	Vicks NyQuil Cold/Flu (cpm)
HBr/acetaminophen/chlorpheniramine maleate dextromethorphan	Diabetic Tussin Night Time
HBr/acetaminophen/diphenhvdramine HCl dextromethorphan	All-Nite Cold-Flu
HBr/acetaminophen/doxylamine dextromethorphan	Cold-Flu Relief
HBr/acetaminophen/doxylamine dextromethorphan	Contac Cold-Flu Night
HBr/acetaminophen/doxylamine dextromethorphan	Coricidin HBP Cold-MultiSympt
HBr/acetaminophen/doxylamine dextromethorphan	Cough-Sore Throat Night
HBr/acetaminophen/doxylamine	
dextromethorphan HBr/acetaminophen/doxylamine	Night Time
dextromethorphan HBr/acetaminophen/doxylamine	Night Time Cold
dextromethorphan	Night Time Cold and FluRelief
HBr/acetaminophen/doxylamine dextromethorphan	Night Time Cold-Flu
HBr/acetaminophen/doxylamine dextromethorphan	Night Time Cold-Flu Relief
HBr/acetaminophen/doxylamine dextromethorphan	Nighttime Cold-Flu
HBr/acetaminophen/doxylamine dextromethorphan	Nighttime Cold-Flu Relief
HBr/acetaminophen/doxylamine dextromethorphan	Nite Time Cold-Flu
HBr/acetaminophen/doxylamine	
dextromethorphan HBr/acetaminophen/doxylamine	Nite Time Cold-Flu Relief
TIBIT GCCCUTTITIONTICTIT GONYTUTTITIC	

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dextromethorphan HB/dextaminophen/doxylamine dextromethorphan HB/dextaminophen/doxylamine dextromethorphan HB/dextaminophen/doxylamine dextromethorphan HB/dextaminophen/doxylamine dextromethorphan HB/dextaminophen/doxylamine dextromethorphan Vicks Nature Fusion Cold-Flu Night HB/dextaminophen/doxylamine dextromethorphan Vicks Nyquil Cold/FluLiquicap HB/dextaminophen/doxylamine dextromethorphan Wicks Nyquil Cold/FluLiquicap HB/dextaminophen/doxylamine dextromethorphan HB/doxylamine succinate dextromethorphan HB/fybenylephrine HCl dextromethorphan HB/doxylamine succinate vicks Nyouli Cough Decomplan HB/doxylamine succinate dextromethorphan HB/doxylamine succinate dextromethorphan HB/doxylamine succinate dextromethorphan HB/doxylamine succinate vicks Nyouli Cough Decomplan HB/doxylamine succinate dextromethorphan HB/doxylamine succinate dextromethorphan HB/doxylamine succinate vicks Nyouli Cough Decomplan HB/doxylamine succinate vicks Nyouli Cough Decomplan HB/doxylamine succinate vicks Nyouli Cough Decomplan	Generic Name	Brand Name
HBI/actaminonhen/doxvlamine dextromethorphan HBI/doxylamine succinate dextromethorphan		
dextromethorphan HBr/dextaminobhen/dowlamine dextromethorphan (Section of the Northern of the	•	
dextromethorphan HBr/acetaminobhen/doxvlamine dextromethorphan HBr/acetaminobhen/doxvlamine dextromethorphan HBr/acetaminobhen/doxvlamine dextromethorphan HBr/acetaminobhen/doxvlamine dextromethorphan HBr/acetaminobhen/doxvlamine HBr/acetaminobhen/doxvlamine HBr/acetaminobhen/doxvlamine HBr/acetaminobhen/doxvlamine succinate dextromethorphan HBr/doxylamine succinate dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl/acetaminoben dextromethorphan HBr/phenylephrine HCl/acetaminoben dextromethorphan HBr/phenylephrine HCl/acetaminoben dextromethorphan HBr/phenylephrine Day Time PE HCl/acetaminoben dextromethorphan HBr/phenylephrine Day Time PE HCl/acetaminoben dextromethorphan HBr/phenylephrine Day time Cold-Flu Relief (PE) HCl/acetaminoben dextromethorphan HBr/phenylephrine Day time Cold-Flu Relief (PE) HCl/acetaminoben dextromethorphan HBr/phenylephrine HCl/acetaminoben HCl/acetaminoben HCl/acetaminoben HCl/acetaminoben HCl/acetaminoben HCl/acetaminoben HCl/		Nitetime Multi-Symptom
HBr/acetaminophen/doxylamine dextromethorphan HBr/acetaminophen/doxylamine dextromethorphan HBr/acetaminophen/doxylamine dextromethorphan HBr/acetaminophen/doxylamine dextromethorphan HBr/acetaminophen/doxylamine dextromethorphan HBr/doxylamine succinate dextromethorphan HBr/phenylephrine HCI dextromethorphan HBr/phenylephrine Cold Head CongestionDaytime HCl/acetaminophen dextromethorphan HBr/phenylephrine Cold-Flu Relief HCl/acetaminophen dextromethorphan HBr/phenylephrine HCl/acetaminophen dextromethorphan HBr/phenylephrine Day Multi-Symp Flu-SevereCold HCl/acetaminophen dextromethorphan HBr/phenylephrine Daytime Cold-Flu HCl/acetaminophen dextromethorphan HBr/phenylephrine Daytime Cold-Flu HCl/acetaminophen dextromethorphan HBr/phenylephrine Daytime Cold-Flu HCl/acetaminophen dextromethorphan HBr/phenylephrine HCl/acetaminophen dextromethorphan HBr/	HBr/acetaminophen/doxylamine	
dextromethorphan HBr/acetaminobhen/doxvlamine dextromethorphan HBr/acetaminobhen/doxvlamine dextromethorphan HBr/acetaminobhen/doxvlamine dextromethorphan HBr/acetaminobhen/doxvlamine HBr/acetaminobhen/doxvlamine HBr/acetaminobhen/doxvlamine HBr/acetaminobhen/doxvlamine succinate dextromethorphan HBr/doxylamine succinate dextromethorphan HBr/phenylephrine HCl children's Cold-CoughDaytime dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine Cold and Cough (pe-dm) dextromethorphan HBr/phenylephrine Cold Hada CongestionDaytime HCl/acetaminobhen dextromethorphan HBr/phenylephrine Cold-Flu Relief HCl/acetaminobhen dextromethorphan HBr/phenylephrine Day Multi-Sympt Flu-SevereCold HCl/acetaminobhen dextromethorphan HBr/phenylephrine Day Time PE HCl/acetaminobhen dextromethorphan HBr/phenylephrine Daytime Cold-Flu Relief (PE) HCl/acetaminobhen dextromethorphan HBr/phenylephrine Daytime Cold-Flu Relief (PE) HCl/acetaminobhen dextromethorphan HBr/phenylephrine HCl/acetaminobhen HCl/acetaminobhen HCl/acetaminobhen HCl/acetaminobhen HCl/acetaminobh	dextromethorphan	Robitussin Cold-Flu Night
HBF/acetaminoohen/doxvlamine dextromethorphan HBF/acetaminoohen/doxvlamine dextromethorphan HBF/acetaminoohen/doxvlamine dextromethorphan HBF/doxylamine succinate dextromethorphan HBF/phenylephrine HCI dextromethorphan HBF/phenylephrine dextromethorphan HBF/phenylephri	HBr/acetaminophen/doxylamine	
dextromethorphan HBr/acetaminoohen/doxvlamine dextromethorphan HBr/doxylamine succinate dextromethorphan HBr/phenylephrine HCl children's Cold-Cough Daytime dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl cold and Cough (pe-dm) dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine HCl/acetaminoohen dextromethorphan HBr/phenylephrine HCl/acetaminoohen dextromethorphan HBr/phenylephrine Day Time PE HCl/acetaminoohen dextromethorphan HBr/phenylephrine HCl/acetaminoohe	dextromethorphan	Vicks Nature Fusion Cold-Flu
HBr/acetaminophen/doxvlamine dextromethorphan HBr/doxvlamine succinate dextromethorphan HBr/phenylephrine HCl Children's Sudafed PE Cough dextromethorphan HBr/phenylephrine HCl dextromethorphan HBr/phenylephrine Cold Head CongestionDaytime HCl/acetaminophen dextromethorphan HBr/phenylephrine Cold Head CongestionDaytime HCl/acetaminophen dextromethorphan HBr/phenylephrine HCl/acetaminophen dextromethorphan HBr/phenylephrine Day Multi-Symptom HCl/acetaminophen dextromethorphan HBr/phenylephrine Day Time PE HCl/acetaminophen dextromethorphan HBr/phenylephrine Daytime Cold HCl/acetaminophen dextromethorphan HBr/phenylephrine Daytime Cold-Flu Relief (PE) HCl/acetaminophen dextromethorphan HBr/phenylephrine HCl/acetaminophen d		
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HCI/acetaminophen dextromethorphan HBr/phenylephrine Mapap Cold Formula HCI/acetaminophen dextromethorphan HBr/phenylephrine Mucinex Fast-MaxCongest-Head		Daytime Cold-Flu Relief (PE)
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HCI/acetaminophen dextromethorphan HBr/phenylephrine HerbioMed Body Aches-SinusM-S HCI/acetaminophen dextromethorphan HBr/phenylephrine HCI/acetaminophen dextromethorphan HBr/phenylephrine Mucinex Fast-MaxCongest-Head		• • •
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HCI/acetaminophen dextromethorphan HBr/phenylephrine Mucinex Fast-MaxCongest-Head		
dextromethorphan HBr/phenylephrine Mucinex Fast-MaxCongest-Head		Mapap Cold Formula
HCI/acetaminophen		Mucinex Fast-MaxCongest-Head
	HCI/acetaminophen	

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Generic Name	Brand Name
dextromethorphan HBr/phenylephrine	Mucinex Fast-MaxSevCold-Sinus
HCl/acetaminophen dextromethorphan HBr/phenylephrine	Robitussin Cold-Flu Day
HCl/acetaminophen dextromethorphan HBr/phenylephrine	Sudafed PEPressure-Pain-Cough
HCl/acetaminophen dextromethorphan HBr/phenylephrine	Theraflu ExpressMax ColdDay
HCl/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
HCI/acetaminophen dextromethorphan HBr/phenylephrine	Vicks DayQuil Cold-Flu Relief
HCI/acetaminophen dextromethorphan HBr/phenylephrine	Vicks Nature Fusion
HCl/acetaminophen dextromethorphan HBr/phenylephrine	Wal-Flu Severe Cold-Cough
HCl/acetaminophen dextromethorphan HBr/phenylephrine	Alahist CF
HCI/dexbrompheniramine	
dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine	Alahist DM
dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine	Bionatuss DXP
dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine	G-P-Tuss DXP
dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine	Supress A
dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine	Alka-Seltzer PlusSin-Allg-Cgh
dextromethorphan	Cold Multi-SymptomNightTime
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Cold and Flu Relief Plus (D/N)
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Cold-Flu Relief, Day/Night
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Daytime-Nighttime
HBr/phenylephrine/acetaminophen/doxylamine 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	Tylenol Cold Max Night
HBr/phenylephrine/acetaminophen/doxylamine	

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Generic Name	Brand Name
dextromethorphan	Tylenol Cold Multi-SymptNight
HBr/phenylephrine/acetaminophen/doxylamine dextromethorphan	Vicks NyQuil Severe Cold-Flu
HBr/phenvlephrine/acetaminophen/doxvlamine dextromethorphan HBr/pseudoephedrine	DAY-TIME
HCI/acetaminophen dextromethorphan HBr/pseudoephedrine	Daytime Cold and Flu Relief
HCI/acetaminophen dextromethorphan/phenylephrine/acetaminophen	HerbioMed Deep Cold-FluNight
/diphenhvdramine dextromethorphan/phenylephrine/acetaminophen	Multi-Symptom SevereCold-Nt
/diphenhvdramine dextromethorphan/pseudoephrine	Alka-Seltzer Plus Cold+Flu
HCl/acetaminophen/doxylamine dextromethorphan/pseudoephrine	Night Time Cold Medicine
HCI/acetaminophen/doxylamine	
dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine	Night Time Cold-Flu
dextromethorphan/pseudoephrine	Night Time Cold-Flu Relief
HCl/acetaminophen/doxvlamine dextromethorphan/pseudoephrine	Nite Time
HCl/acetaminophen/doxylamine diclofenac sodium	diclofenac sodium
diphenhydramine HCl	Alka-Seltzer Plus Allergy
diphenhydramine HCl	Aller-G-Time
diphenhydramine HCl	Allergy
diphenhydramine HCl	Allergy (diphenhydramine)
diphenhydramine HCl	Allergy Medication
diphenhydramine HCl	Allergy Medicine
diphenhydramine HCl	AllergyRelief(diphenhydramin)
diphenhydramine HCl	Banophen
diphenhydramine HCl	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	Children's Benadryl Allergy
diphenhydramine HCl	Children's Diphenhydramine
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

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Generic Name	Brand Name
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 HCI/hydrocortisone	HC Derma-Pax
diphenhydramine HCl/phenylephrine	Adult Robitussin Night M-SCld
HCI/acetaminophen	All AACAR Luc
diphenhydramine HCl/phenylephrine	Allergy M-S Nighttime
HCI/acetaminophen	Allergy Phys Covers Cinus IIA
diphenhydramine HCl/phenylephrine	Allergy Plus Severe Sinus HA
HCI/acetaminophen diphenhydramine HCI/phenylephrine	Allergy Sinus Headache (PE)
HCI/acetaminophen	Allergy Silius riedudche (FL)
diphenhydramine HCI/phenylephrine	Allergy and Cold PE
HCI/acetaminophen	Allergy and Cold FE
diphenhydramine HCl/phenylephrine	Child Delsym Cough+Cold
HCI/acetaminophen	Cilia Deisyin Coagni Cola
diphenhydramine HCl/phenylephrine	Children Dimetapp M-SCold-Flu
HCI/acetaminophen	emaren ametapp w sedia na
diphenhydramine HCl/phenylephrine	Children's Mucinex NightTime
HCI/acetaminophen	emaren a waemex warenne
diphenhydramine HCI/phenylephrine	Cold and FluRelief(diphen-pe)
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Cough and Severe Cold
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Delsym Cough-ColdNightTime
HCI/acetaminophen	, 5
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Generic Name	Brand Name
diphenhydramine HCI/phenylephrine	Flu Relief Therapy Nighttime
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Flu and Sore Throat Relief
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Flu-Severe Cold-Cough Night
HCI/acetaminophen diphenhydramine HCI/phenylephrine	Herbiomed Allergy Cold-Sinus
HCI/acetaminophen	Herbiotilea Allergy Cola-Silius
diphenhydramine HCI/phenylephrine	Mucinex Fast-Max NiteCold-Flu
HCI/acetaminophen	
diphenhydramine HCI/phenylephrine	Mucinex Sinus-Max NiteCongest
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Severe Allergy-SinusHeadache
HCI/acetaminophen	Carrage Cald Carral Eliz
diphenhydramine HCl/phenylephrine	Severe Cold Cough-Flu
HCI/acetaminophen diphenhydramine HCI/phenylephrine	Severe Cold PE
HCI/acetaminophen	Severe colu i E
diphenhydramine HCl/phenylephrine	Theraflu ExpressMax ColdNight
HCI/acetaminophen	, G
diphenhydramine HCI/phenylephrine	Theraflu Night SevereCold-Cgh
HCI/acetaminophen	
diphenhydramine HCl/phenylephrine	Theraflu Nighttime PowerPod
HCI/acetaminophen	Wal Dayl Cayona Allanay Ciaya
diphenhydramine HCl/phenylephrine	Wal-Dryl Severe Allergy-Sinus
HCI/acetaminophen diphenhydramine HCI/phenylephrine	Wal-Flu Severe Cold andCough
HCI/acetaminophen	Wal the severe sold undesdagin
diphenhydramine HCl/phenylephrine	Wal-phed PE Severe Cold
HCl/acetaminophen	
diphenhydramine HCl/phenylephrine	Child Cold-Cough Day-Night
HCI/dextromethorphan HBr	
diphenhydramine	Sinus Relief Max StrDay-Night
HCI/phenylephrine/acetaminophen/guaifenesin diphenhydramine/phenylephrin/dextromethorph	Children's M-S ColdDay-Night
/acetaminophen/GG	Cilidren's W-5 Cold Day Wight
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	Clantucs
doxylamine succ/pseudoephedrine HCl/dextromethorphan Hbr	Glentuss
doxylamine succ/pseudoephedrine	Lortuss DM
HCI/dextromethorphan Hbr	20.0000 2111
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 LQ
doxylamine/phenylephrine/dextromethorphan	Day-Nite Severe Cold-Flu
/acetaminophen/GG	

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Generic Name	Brand Name
doxylamine/phenylephrine/dextromethorphan	Mucinex Fast-MaxDay-Nt(doxyl)
/acetaminophen/GG	, , , ,
doxylamine/phenylephrine/dextromethorphan	Mucinex Sinus-Max Dy-Nt(dxyl)
/acetaminophen/GG	
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)
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 HCl/pseudoephedrine HCl	Allergy Relief-D(fexofenadine)
fexofenadine HCl/pseudoephedrine HCl	Allergy-CongestRelief-D(fexo)
fexofenadine HCl/pseudoephedrine HCl	Wal-Fex D 12 Hour

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Appendix of centeric and prairie france of incured in council of	
Generic Name	Brand Name
fexofenadine HCI/pseudoephedrine HCI	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	<u>-</u>
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 RIf
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
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

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Generic Name	Brand Name
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
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	lophen DM-NR
guaifenesin/dextromethorphan HBr	Medi-Tussin DM
guaifenesin/dextromethorphan HBr	Medi-Tussin DM Diabetic

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Generic Name	Brand Name
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
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
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Generic Name guaifenesin/dextromethorphan HBr/phenylephrine guaifenesin/
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guaifenesin/dextromethorphan HBr/phenylephrine Mucinex Fast-MaxCongest-Cough Mucus ReliefCongestion-Cough
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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

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guaifenesin/dextromethorphan HBr/phenylephrine guaifenesin/dextromethorphan HBr/phassium citrate guaifenesin/dextromethorphan HBr/phassium citrate guaifenesin/dextromethorphan Actinel Pediatric HBr/pseudoenbedrine HCI guaifenesin/dextromethorphan Actinel Pediatric HBr/pseudoenbedrine HCI guaifenesin/dextromethorphan Bionel HBr/pseudoenbedrine HCI guaifenesin/dextromethorphan Bionel Pediatric Buaifenesin/dextromethorphan Br/pseudoenbedrine HCI guaifenesin/dextromethorphan Tusnel DMPediatric(pseudoeph) Br/pseudoenbedrine HCI guaifenesin/dextromethorphan Tusnel DMPediatric(pseudoeph) Br/pseudoenbedrine HCI guaifenesin/dextromethorphan Tusnel Pediatric Buaifenesin/dextromethorphan Tusnel Pediatric Buaifenesin/dextromethorphan Tusnel Pediatric Buaifenesin/dextrometh	Generic Name	Brand Name
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guaifenesin/dextromethorphan HBr/oseudoenbedrine HCI guaifenesin/dextromethorphan HBr	•	Actinei Pediatric
guaifenesin/dextromethorphan HBr/oseudoenhedrine HCI guaifenesin/dextromethorphan HBr		Ambi 40PSE-400GFN-20DM
HBr/pseudoephedrine HCl guaifenesin/dextromethorphan HBr/sseudoephedrine HCl guaifenesin/dextromethorphan HBr/sseudoephedrine HCl guaifenesin/dextromethorphan HBr/pseudoephedrine HCl guaifenesin/dytphylline		Bionel
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		Difil-G 400
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guaifenesin/hydrocodone bitartrate Flowtuss		
guaifenesin/hydrocodone bitartrate Obredon		Obredon

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gualfenesin/phenylephrine HCI gualfenesin/phenylephrine HCI/acetaminophen gualfenesin/phenylephrine HCI/acetaminophen gualfenesin/phenylephrine HCI/acetaminophen gualfenesin/phenylephrine HCI/acetaminophen gualfenesin/phenylephrine HCI/acetaminop	Generic Name	Brand Name
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guaifenesin/phenylephrine HCl/acetaminophen guaifenesin/pseudoephedrine HCl Despec-Tab	guaifenesin/phenylephrine HCl/acetaminophen	Pressure-Pain PE Plus Mucus
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guaifenesin/phenylephrine HCl/acetaminophen guaifenesin/pseudoephedrine HCl Despec-Tab	guaifenesin/phenylephrine HCl/acetaminophen	Severe Sinus
guaifenesin/phenylephrine HCl/acetaminophen guaifenesin/pseudoephedrine HCl Despec-Tab	guaifenesin/phenylephrine HCl/acetaminophen	Sinus Congestion-Pain(guaif)
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guaifenesin/pseudoephedrine HCl Despec-Tab	guaifenesin/phenylephrine HCl/acetaminophen	Tylenol Sinus CongestionPain
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guaifenesin/pseudoephedrine HCl Despec-Tab		Congest-Eze
	guaifenesin/pseudoephedrine HCl	Congestac
guaifenesin/nseudoenhedrine HCl Fntex T	guaifenesin/pseudoephedrine HCl	Despec-Tab
Enter 1	guaifenesin/pseudoephedrine HCl	Entex T

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Generic Name	Brand Name
guaifenesin/pseudoephedrine HCl	ExeFen-IR
guaifenesin/pseudoephedrine HCl	Maxifed
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
uaifenesin/pseudoephedrine HCl	Triacting Expectorant
uaifenesin/pseudoephedrine HCl	Tusnel Pediatric
guaifenesin/pseudoephedrine HCl	pseudoephedrine-guaifenesin
nalobetasol propionate/ammonium lactate	Halonate
nalobetasol propionate/ammonium lactate	Halonate Pac
alobetasol propionate/ammonium lactate	Ultravate PAC
alobetasol propionate/lactic acid	Ultravate X
ydrocodone bitartrate/chlorpheniramine maleate	Vituz
ydrocodone bitartrate/homatropine	Hydrocodone Compound
methvlbromide	
nydrocodone bitartrate/homatropine	Hydromet
methylbromide	
nydrocodone bitartrate/homatropine	Tussigon
methylbromide	
nydrocodone bitartrate/homatropine	hydrocodone-homatropine
methylbromide	
nydrocodone bitartrate/pseudoephedrine	Hycofenix
HCI/guaifenesin	
nydrocodone polistirex/chlorpheniramine polistirex	TussiCaps
nydrocodone polistirex/chlorpheniramine polistirex	Tussionex Pennkinetic ER
nydrocodone polistirex/chlorpheniramine polistirex	hydrocodone-chlorpheniramine
nydrocortisone	Cortef
nydrocortisone	hydrocortisone
nydrocortisone acetate/aloe vera	Nucort
nydrocortisone acetate/aloe vera	hydrocortisone acet-aloe vera
nydrocortisone acetate/pramoxine HCl	Analpram-HC
nydrocortisone acetate/pramoxine HCl	Epifoam
nydrocortisone acetate/pramoxine HCl	Mezparox-HC
nydrocortisone acetate/pramoxine HCl	Novacort
nydrocortisone acetate/pramoxine HCl	Pramosone
nydrocortisone acetate/pramoxine HCl	hydrocortisone-pramoxine
nydrocortisone acetate/pramoxine HCl/aloe	Novacort (with aloe)
polysaccharide	
nydrocortisone acetate/pramoxine HCI/emollient	Pramosone E
pase	
nydrocortisone acetate/urea	U-Cort
nydrocortisone sod succinate	A-Hydrocort
nydrocortisone sod succinate	Solu-Cortef
nydrocortisone sodium succinate/PF	Solu-Cortef Act-O-Vial (PF)
nydrocortisone/aloe vera	Anti-Itch(hydrocortisone)-Aloe
nydrocortisone/aloe vera	Cortisone with Aloe
ydrocortisone/aloe vera	Cortizone-10 with aloe
•	
nydrocortisone/aloe vera nydrocortisone/aloe vera	Hydrocortisone Plus Hydroskin with Aloe

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Addaprin Buprofen
hydrocortisone/aloe vera/vitamin E acetate/vitamins A and D hydrocortisone/aloe vera/vitamin E acetate/vitamins A and D hydrocortisone/emollient combination no.45 hydrocortisone/emollient combination no.45 hydrocortisone/emollient combination no.25 hydrocortisone/emineral oil/petrolatum,white hydrocortisone/skin cleanser combination no.25 hydrocortisone/skin cleanser combination no.35 byermasorb HC Complete Kit ibuprofen ibuprofen/diphenhydramine HCl ibuprofen-diphenhydramine HCl ibuprofen-diphenhydramine HCl ibuprofen/phenylephrine HCl i
acetate/vitamins A and D hydrocortisone/aloe vera/vitamin E acetate/vitamins A and D hydrocortisone/emollient combination no.45 hydrocortisone/mineral oil/petrolatum,white hydrocortisone/mineral oil/petrolatum,white hydrocortisone/skin cleanser combination no.25 hydrocortisone/skin cleanser combination no.35 Dermasorb HC Complete Kit ibuprofen Belipenhydramine HCI ibuprofen-diphenhydramine HCI ibuprofen-diphenhydramine HCI ibuprofen/phenylephrine HCI ibuprofen/p
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hydrocortisone/emollient combination no.45 hydrocortisone/mineral oil/petrolatum,white hydrocortisone/skin cleanser combination no.25 hydrocortisone/skin cleanser combination no.35 hydrocortisone/skin cleanser combination no.35 bermasorb HC Complete Kit ibuprofen ibuprofen/diphenhydramine HCl ibuprofen/diphenhydramine ictrate ibuprofen/diphenhydramine ictrate ibuprofen/phenylephrine HCl ibuprofen/phenylephrine HCl ibuprofen/phenylephrine HCl ibuprofen/pseudoephedrine HCl ibuprofen/goeudoephedrine HCl
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hydrocortisone/skin cleanser combination no.25 hydrocortisone/skin cleanser combination no.35 ibuprofen ibuprofen/diphenhydramine HCl ibuprofen/diphenhydramine HCl ibuprofen/diphenhydramine itrate ibuprofen/phenylephrine HCl ibuprofen/phenylephrine HCl ibuprofen/phenylephrine HCl ibuprofen/phenylephrine HCl ibuprofen/pseudoephedrine HCl Advil Congestion Relief ibuprofen-PE) ibuprofen/pseudoephedrine HCl Advil Cold and Sinus
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ibuprofen/phenylephrine HCl ibuprofen/phenylephrine HCl ibuprofen/pseudoephedrine HCl Advil Congestion Relief Congestion Relief(ibuprof-PE) Advil Cold and Sinus
ibuprofen/phenylephrine HCl Congestion Relief(ibuprof-PE) ibuprofen/pseudoephedrine HCl Advil Cold and Sinus
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
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 (bulk)
levalbuterol tartrate Xopenex HFA

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Generic Name	Brand Name
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
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

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Generic Name	Brand Name
methylprednisolone acetate in sodium	methylpredac(PF)-NaCl,iso-osm
chloride,iso-osmotic/PF	
methylprednisolone acetate in sterile water for	methylprednisoloneacet-water
injection	Dharisiana 57 Has MA Duad
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
mometasone furoate/formoterol fumarate	Dulera
montelukast sodium	Singulair
montelukast sodium	montelukast
montelukast sodium	montelukast (bulk)
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 HCl/acetaminophen	AcetaminophenCongestion-Pain
phenylephrine HCl/acetaminophen	Contac Cold-Flu Day
phenylephrine HCl/acetaminophen	DayTime Sinus Congestion
phenylephrine HCl/acetaminophen	Daytime Sinus-Congestion Manan Sinus May Strongth (DE)
phenylephrine HCl/acetaminophen phenylephrine HCl/acetaminophen	Mapap Sinus Max Strength(PE) Non-Aspirin Sinus
phenylephrine HCl/acetaminophen	Pain Relief Sinus PE
phenylephrine HCl/acetaminophen	Pyrroxate Cold andCongestion
phenylephnine ner/acetaninophen	i yiioxate colu aliucoligestioli

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Type name of control and branch trained of the and the control of	
Generic Name	Brand Name
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
phenylephrine HCl/acetaminophen	Wal-Phed PE SinusHeadache
phenylephrine	Allergy Multi-Symptom
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Allergy Relief Multi-Symptom
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Allergy Relief(chlorphen-acet)
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Allergy Sinus PE
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Contac Cold-Flu Day andNight
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Contac Cold-Flu Max Strength
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Dristan Cold
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Effervescent Cold Relief Plus
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Medicidin-D
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Norel AD
HCI/acetaminophen/chlorpheniramine	
phenylephrine	Sinus Congest-PainDay-Night
HCI/acetaminophen/chlorpheniramine	
phenylephrine	SinusCongestion-Pain(chlorph)
HCI/acetaminophen/chlorpheniramine	6
phenylephrine	Sinutrol PE
HCl/acetaminophen/chlorpheniramine	Des Times and Alike Times Cines
phenylephrine HCI/acetaminophen/doxylamine	DayTime and NiteTime Sinus
succinate	NijelaTira a Circus
phenylephrine HCI/acetaminophen/doxylamine	NightTime Sinus
succinate	Niehttine Cieve Congestion
phenylephrine HCI/acetaminophen/doxylamine	Nighttime Sinus-Congestion
succinate	C. D. C. Miller
phenylephrine HCI/acetaminophen/doxylamine	Sinus Daytime-Nightime
succinate	ACL AL CIG
phenylephrine HCI/acetaminophen/doxylamine	Vicks Nyquil Sinex
succinate	Minha Olasa Osil Ninhai
phenylephrine HCI/acetaminophen/doxylamine	Vicks QlearQuil NightimeSinus
succinate	Daniel Landin De dietaie
phenylephrine HCl/chlophedianol HCl/guaifenesin	Donatussin Pediatric
phenylephrine HCl/chlophedianol HCl/guaifenesin	Vanacof GPE

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Generic Name	Brand Name
phenylephrine HCI/chlophedianol HCI/guaifenesin	phenylephrine-chlophedianol-GG
phenylephrine HCl/codeine	Phenflu CD
phosphate/acetaminophen/guaifen phenylephrine HCl/codeine	Phenflu CDX
phosphate/acetaminophen/guaifen	Flielilla CDX
shenylephrine HCI/dextromethorphan	Children's Cold-Cough-Sore
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Children's MucinexCold-Fever
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Cold Head Congestion SeverDay
HBr/acetaminophen/guaifen	
phenylephrine HCI/dextromethorphan	Cold Severe Congestion
lBr/acetaminophen/guaifen henylephrine HCl/dextromethorphan	Cold and Flu Severe
HBr/acetaminophen/guaifen	cold and the severe
phenylephrine HCI/dextromethorphan	Cold-Cough Sinus Relief PE
IBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Decorel Forte Plus
Br/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Delsym Cough-Cold Daytime
HBr/acetaminophen/guaifen	Demotuse C
henylephrine HCl/dextromethorphan	Dometuss G
IBr/acetaminophen/guaifen henylephrine HCl/dextromethorphan	Fast Mucus Relief SevereCold
IBr/acetaminophen/guaifen	ruse wideds heller severeesta
henylephrine HCl/dextromethorphan	Head Congestion Cold Relief
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Herbiomed Severe Cold-FluM-S
HBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Mucinex Cold,Flu,Sore Throat
lBr/acetaminophen/guaifen henylephrine HCl/dextromethorphan	Mucinex Fast-MaxCold-Flu-Thrt
HBr/acetaminophen/guaifen	Muchex rast-Maxeou-Flu-Till t
phenylephrine HCl/dextromethorphan	Mucinex Fast-Max SevereCold
HBr/acetaminophen/guaifen	
henylephrine HCl/dextromethorphan	Mucinex Sinus-MaxPressure-Cgh
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Mucinex Sinus-Max SevCong(DM)
HBr/acetaminophen/guaifen henylephrine HCl/dextromethorphan	Mucus Relief Cold-Flu-SoreThr
nenylephrine HCI/dextromethorphan IBr/acetaminophen/guaifen	ואומרמי עבוובו רחומ-בומ-סחוב וווו
phenylephrine HCl/dextromethorphan	Mucus Relief Plus
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Mucus Relief SevCongest-Cold
HBr/acetaminophen/guaifen	
henylephrine HCI/dextromethorphan	Mucus Relief Severe Cold
HBr/acetaminophen/guaifen	Multi Consultani C. LL (55)
phenylephrine HCl/dextromethorphan	Multi-Symptom Cold (PE)
HBr/acetaminophen/guaifen ohenylephrine HCl/dextromethorphan	Non-Pseudo Cold Relief
HBr/acetaminophen/guaifen	Horr i seddo cold ficilei
br/acetammopnen/guairen	

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Generic Name	Brand Name
phenylephrine HCI/dextromethorphan	Pain Relief Cold
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Pressure-Pain PE Plus Cold
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Pressure-Pain-Cold
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Rompe Pecho Max MultiSymptoms
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Severe Cold
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Severe Cold Multi-Symptom
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Severe Cold and Flu (PE)
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Sudafed PEPressure-Pain-Cold
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Tussin CF Max Severe M-SCold
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Tylenol Cold and Flu Severe
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Vicks DayQuil SevereCold-Flu
HBr/acetaminophen/guaifen phenylephrine HCl/dextromethorphan	Wal-Phed PE Cold-Cough
HBr/acetaminophen/guaifen 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 HCI/diphenhydramine HCI	Children Night TimeCold-Cough
phenylephrine HCI/diphenhydramine HCI	Childs Triacting Cold-Cough
phenylephrine HCI/diphenhydramine HCI	Cold and Cough(diphenhydr-pe)
phenylephrine HCI/diphenhydramine HCI	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 promethazine-phenylephrine
phenylephrine HCl/promethazine HCl phenylephrine HCl/pyrilamine maleate	Aldex D
phenylephrine HCI/pyrilamine maleate	Glen PE
phenylephrine HCl/pyrilamine maleate	Poly Hist Forte (pyrilamine)
phenylephrine HCl/pyrilamine maleate	Pyril D
phenylephrine HCI/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

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Generic Name	Brand Name
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
pseudoephedrine	Allergy Sinus-D
HCI/acetaminophen/chlorpheniramine	
pseudoephedrine	Non-Aspirin Allergy Sinus
HCI/acetaminophen/chlorpheniramine	
pseudoephedrine	Non-Aspirin Child's Cold
HCI/acetaminophen/chlorpheniramine pseudoephedrine	Pain Reliever Allergy Sinus
HCI/acetaminophen/chlorpheniramine	
pseudoephedrine HCl/acrivastine	Semprex-D
pseudoephedrine HCl/chlophedianol HCl	Rondec-D
pseudoephedrine HCI/chlophedianol	Certuss-D
HCI/guaifenesin	
pseudoephedrine HCl/chlophedianol	Vanacof DX
HCI/guaifenesin	
pseudoephedrine HCl/chlophedianol	Vanatab DX
HCl/guaifenesin pseudoephedrine HCl/chlorpheniramine	Respa-AR
maleate/bellad alk	·
pseudoephedrine HCI/codeine phosphate	Codar D
pseudoephedrine HCI/codeine	Maxiflu CD
phosphate/acetaminophen/guaifen	
pseudoephedrine HCl/codeine	Maxiflu CDX
phosphate/acetaminophen/guaifen	
pseudoephedrine HCl/codeine	Cheratussin DAC
phosphate/guaifenesin	
pseudoephedrine HCl/codeine	Coditussin DAC
phosphate/guaifenesin	
pseudoephedrine HCl/codeine	Guaifenesin DAC
phosphate/guaifenesin	
pseudoephedrine HCI/codeine	Lortuss EX
phosphate/guaifenesin	

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Generic Name	Brand Name
pseudoephedrine HCI/codeine	Phenylhistine
phosphate/guaifenesin	,
pseudoephedrine HCI/codeine	Tricode GF
phosphate/guaifenesin	
pseudoephedrine HCl/codeine	Tusnel C
phosphate/guaifenesin	
pseudoephedrine HCI/codeine	Virtussin DAC
phosphate/guaifenesin	
pseudoephedrine HCI/codeine	Zodryl DEC 25
phosphate/guaifenesin	7
pseudoephedrine HCl/codeine	Zodryl DEC 30
phosphate/guaifenesin	Zodnil DEC 25
pseudoephedrine HCl/codeine	Zodryl DEC 35
phosphate/guaifenesin pseudoephedrine HCI/codeine	Zodryl DEC 40
phosphate/guaifenesin	20di yi DEC 40
pseudoephedrine HCl/codeine	Zodryl DEC 50
phosphate/guaifenesin	2001,11,220,30
pseudoephedrine HCI/codeine	Zodryl DEC 60
phosphate/guaifenesin	•
pseudoephedrine HCl/codeine	Zodryl DEC 80
phosphate/guaifenesin	
pseudoephedrine HCl/codeine/chlorpheniramine	Phenylhistine DH
pseudoephedrine HCI/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 pyrilamine maleate/chlophedianol	Vanacof-8 Ninjacof-A
HCl/acetaminophen	Nilljacor-A
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 roflumilast	Yupelri Daliresp
salmeterol xinafoate	Daliresp Serevent Diskus
terbutaline sulfate	terbutaline
theophylline anhydrous	Elixophyllin
theophylline anhydrous	Theo-24
	- :

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Generic Name	Brand Name
theophylline anhydrous	Theochron
theophylline anhydrous	theophylline
thonzylamine HCl/chlophedianol HCl	POLY HIST PD
thonzylamine HCl/phenylephrine HCl	Nasopen PE
thonzylamine HCl/phenylephrine	Vanacof APE
HCI/chlophedianol HCl	Valiacol Al E
thonzylamine HCl/phenylephrine	Poly-Hist DM (thonzylamine)
HCI/dextromethorphan HBr	1 dry-1113t Divi (thonzylamine)
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	Kenalog
triamcinolone acetonide	Kenalog-80
triamcinolone acetonide	Nasacort
triamcinolone acetonide	Nasacort AQ
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	
triamcinolone acetonide/dimethicone/silicone,	Tri-Sila
adhesive	
triamcinolone acetonide/dimethicone/silicone,	Whytederm TDPak
adhesive	, -
triamcinolone acetonide/dimethicone/silicone,	Whytederm Trilasil Pak
adhesive	,
triamcinolone acetonide/emollient combination	Pediaderm TA
no.45	

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Generic Name	Brand Name
triamcinolone acetonide/emollient combination	Dermasorb TA Complete Kit
no.86	·
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	triamcinolonedia(PF)-0.9%NaCl
chloride/PF	,
triamcinolone hexacetonide	Aristospan Intra-Articular
triamcinolone hexacetonide	Aristospan Intralesional
triamcinolone hexacetonide	triamcinolone hexaceton(bulk)
triamcinolone hexacetonide, micronized	triamcin hexacet, micro (bulk)
triamcinolone/norflurane and pentafluoropropane	P-Care K40G
(HFC 245fa)	
triamcinolone/norflurane and pentafluoropropane	P-Care K80G
(HFC 245fa)	
triamcinolone/norflurane and pentafluoropropane	Pod-Care 100KG
(HFC 245fa)	
triamcinolone/norflurane and pentafluoropropane	Triloan II SUIK
(HFC 245fa)	
triamcinolone/norflurane and pentafluoropropane	Triloan SUIK
(HFC 245fa)	can com
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	HISTEX-AC
triprolidine HCl/phenylephrine	Histex DM
HCI/dextromethorphan HBr	THISTEX DIVI
triprolidine HCl/pseudoephedrine HCl	Aprodine
triprolidine HCl/pseudoephedrine	Trymine CD
	Tryffillie CD
HCI/chlophedianol HCl umeclidinium bromide	Incruse Ellipta
umeclidinium bromide/vilanterol trifenatate	Anoro Ellipta
zafirlukast	Accolate
zafirlukast	zafirlukast
zileuton	
	Zyflo
zileuton	Zyflo CR
zileuton Nonsteroidal Anti-Inflamr	zileuton

Nonsteroidal Anti-Inflammatory Drugs (NSAID)

CHLORPHENIRAMINE Advil Allergy-Congestion Rlf

MALEATE/PHENYLEPHRINE HCL/IBUPROFEN

CHLORPHENIRAMINE

MALEATE/PSEUDOEPHEDRINE

HCI /IBUPROFFN

Advil Allergy Sinus

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HYDROCODONE/IBUPROFEN HYDROCODONE HUBUROFEN/OXYCODONE HUBUROFEN/OXYC	Generic Name	Brand Name
HYDROCODONE/BUPROFEN Victorofen HYDROCODONE/BUPROFEN Xylon 10 HYDROCODONE/BUPROFEN Xylon 10 HYDROCODONE/BUPROFEN Xylon 10 HYDROCODONE/BUPROFEN Hydrocodone-ibuprofen BUPROFEN		
HYDROCODONE/BUPROFEN X/On 10 HYDROCODONE/BUPROFEN A/On 10 HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HYDROCODONE HCL BUPROFEN/PENYLEPHRINE HCL A/ON (Congestion Relief BUPROFEN/PHENYLEPHRINE HCL A/ON (Congestion Relief BUPROFEN/PHENYLEPHRINE HCL CONGESTION RElief (BUPROFEN/PESUDOEPHEDRINE HCL COID and Sinus Pain Relief BUPROFEN/PSEUDOEPHEDRINE HCL COID and Sinus Pain Relief BUPROFEN/PSEUDOEPHEDRINE HCL BUPROFEN/PSEUDOEPHEDRINE APPROXEN SODIUM/PSEUDOEPHEDRINE APPROXEN SODIUM/PSEUDOEPHEDRIN	·	
HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HYDROCODONE/BUPROFEN HUDROFEN HUDROFEN HUDROFEN HUDROFEN HUDROFEN HUDROFEN HUDROFEN HUDROFEN/OXYCODONE HCL HUDROFEN/OXYCODONE HCL HUDROFEN/PHENYLEPHRINE HCL HUDROFEN/PHENYLEPHRINE HCL HUDROFEN/PSEUDOEPHEDRINE Aleve-D Sinus and Headache HCL HCL HUDROFEN/PSEUDOEPHEDRINE Aleve-D Sinus and Cold-D HUDROFEN/PSEUDOEPHEDRINE HCL HUDRO		•
HYDROCODONE/IBUPROFEN Children's Ibuprofen IBUPROFEN/PERNYEPHRINE HCL Ibuprofen-oxycodone IBUPROFEN/PHENYEPHRINE HCL Advil Congestion Relief IBUPROFEN/PHENYEPHRINE HCL Congestion Relief IBUPROFEN/PERNYEPHRINE HCL Congestion Relief IBUPROFEN/PSEUDOEPHEDRINE HCL Cold and Sinus IBUPROFEN/PSEUDOEPHEDRINE HCL Cold and Sinus Pain Relief IBUPROFEN/PSEUDOEPHEDRINE HCL Ibuprofen Cold IBUPROFEN/PSEUDOEPHEDRINE HCL Ibuprofen Cold IBUPROFEN/PSEUDOEPHEDRINE HCL Ibuprofen Cold IBUPROFEN/PSEUDOEPHEDRINE HCL Ibuprofen Cold Sinus (withPSE) IBUPROFEN/PSEUDOEPHEDRINE HCL Ibuprofen Cold Sinus IBUPROFEN/PSEUDOEPHEDRINE HCL Ibuprofen Cold Sinus IBUPROFEN/PSEUDOEPHEDRINE HCL IBUPROFEN PSEUDOEPHEDRINE HCL IBUPROFEN PSEUDOEPHEDRINE HCL IBUPROFEN PSEUDOEPHEDRINE HCL INDOMETHACIN Indomethacin NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Cold and Sinus INDOMETHACIN INDOMETHACI	•	·
IBUPROFEN IBUPROFEN IBUPROFEN/OXYCODONE HCL IBUPROFEN/OXYCODONE HCL IBUPROFEN/OXYCODONE HCL IBUPROFEN/PLENYLEPHRINE HCL IBUPROFEN/PHENYLEPHRINE HCL IBUPROFEN/PHENYLEPHRINE HCL IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Cold and Sinus HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Sinus and Headache HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold-D HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Headache Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celeforac podassium Cidofenac sodium/misoprostol Cidofenac so	•	· · · · · · · · · · · · · · · · · · ·
IBUPROFEN ibupro	·	
IBUPROFEN/OXYCODONE HCL IBUPROFEN/PHENYLEPHRINE HCL IBUPROFEN/PHENYLEPHRINE HCL IBUPROFEN/PHENYLEPHRINE HCL IBUPROFEN/PESUDOEPHEDRINE HCL IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Cold and Sinus Indomethacin NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Sinus and Headache HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Headache HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Headache HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Headache HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold-D HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold-D HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold-D HCL OXAPROZIN piroxicam SINUSATRIPITAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celeforac potassium Citofenac potassium Citofenac potassium Citofenac potassium Citofenac sodium/misoprostol Citofenac etadolac Cetodolac Cetodo		·
IBUPROFEN/PHENYLEPHRINE HCL IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN INDOMETHAC		· · · · · · · · · · · · · · · · · · ·
IBUPROFEN/PHENYLEPHRINE HCL IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Cold and Sinus Indomethacin NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Cold and Sinus APROXEN SODIUM/PSEUDOEPHEDRINE Aleve Dsinus and Headache HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Dsinus and Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Dsinus and Headache HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Dsinus and Cold -D HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve Dsinus and Cold -D HCL COLD SINUS AND	•	
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IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN NAPROXEN SODIUM NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Sinus and Cold-D HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL CL NAPROXEN SODIUM/PSEUDOEPHEDRINE SInus and Cold-D HCL OXAPROZIN OXAPROZIN OXAPROZIN PIROXICAM PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM Celecoxib Celeforac potassium Catafiam Cilcifenac potassium Catafiam Cilcifenac potassium Catafiam Cilcifenac sodium/misoprostol Catafiam Cilcifenac sodium/misoprostol Catafiam Cilcifenac sodium/misoprostol Catafiam Cilcifenac sodium/misoprostol Cilcifenac sodium	-	
IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN INDOMETHACIO INDOMETH		
IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN NAPROXEN SODIUM NAPROXEN SODIUM NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib celecoxib celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium Feno	•	
BUPROFEN/PSEUDOEPHEDRINE HCL Buprofen Cold-Sinus (withPSE) BUPROFEN/PSEUDOEPHEDRINE HCL Wal-Profen D Cold and Sinus Indomethacin	•	
IBUPROFEN/PSEUDOEPHEDRINE HCL IBUPROFEN/PSEUDOEPHEDRINE HCL IBUPROFEN/PSEUDOEPHEDRINE HCL IBUPROKEN SODIUM NAPROXEN SODIUM NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROXIN PIROXICAM piroxicam SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib Combia diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac sodium/misopr	•	•
IBUPROFEN/PSEUDOEPHEDRINE HCL INDOMETHACIN Indomethacin NAPROXEN SODIUM NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN OXAPROZIN OXAPROZIN OXAPROZIN SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Celecoxib Ciclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac sodium/mis		
INDOMETHACIN NAPROXEN SODIUM/ NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL SOXAPROZIN OXAPROZIN PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib celecoxib celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac sodium	·	
NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE All Day Pain Relief Sinus, Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN OXAPROZIN OXAPROZIN OXAPROZIN OXAPROZIN FIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib celecoxib celecoxib diclofenac potassium Cambia diclofenac potassium Cambia diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac so	•	
NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE Aleve-D Sinus and Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE All Day Pain Relief Sinus, Cold HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN OXAPROZIN OXAPROZIN OXAPROZIN OXAPROZIN FIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib celecoxib celecoxib diclofenac potassium Cambia diclofenac potassium Cambia diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac so	NAPROXEN SODIUM	naproxen sodium
HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN Oxaprozin PIROXICAM PIroxicam SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol	NAPROXEN SODIUM/PSEUDOEPHEDRINE	
NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL Sinus and Cold-D HCL OXAPROZIN OXAPROZIN PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib celecoxib celecoxib diclofenac potassium diclofenac sodium/misoprostol diclof	•	
HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN PIROXICAM piroxicam SUMATRIPTAN SUCCINATE/NAPROXEN Treximet SODIUM celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol	-	Aleve Sinus and Headache
NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN PIROXICAM piroxicam SUMATRIPTAN SUCCINATE/NAPROXEN Teximet SODIUM celecoxib celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac s	•	
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NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac fenoprofen calcium fenoprofen calcium fenoprofen calcium fenoprofen calcium fenoprofen calcium Profeno All Day Pain Relief Sinus, Cold And Cold-D Sinus and Cold-D And Cold-D Sinus and Headache All Day Pain Relief Sinus, Cold And Cold-D Sinus and Colde Sinus and Colde Sinus and Colde Sinus and Colde Sinus	•	
HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN PIROXICAM PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol Nalfon fenoprofen calcium		Aleve-D Sinus and Headache
NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN PIROXICAM PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN Celecoxib celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac etodolac etodolac etodolac fenoprofen calcium fenoprofen calcium fenoprofen calcium ProFeno	•	
HCL NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL OXAPROZIN PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/nisoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac etodolac fenoprofen calcium fenoprofen calcium fenoprofen calcium fenoprofen calcium ProFeno	NAPROXEN SODIUM/PSEUDOEPHEDRINE	All Day Pain Relief Sinus,Cold
HCL OXAPROZIN PIROXICAM PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM celecoxib celecoxib diclofenac potassium diclofenac sodium Arthrotec 50 diclofenac sodium/misoprostol diclofenac s	HCL	
OXAPROZIN PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM celecoxib celecoxib diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium	NAPROXEN SODIUM/PSEUDOEPHEDRINE	Sinus and Cold-D
PIROXICAM SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM celecoxib celecoxib celecoxib diclofenac potassium diclofenac sodium diclofenac sodium diclofenac sodium diclofenac sodium diclofenac sodium diclofenac sodium diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium	HCL	
SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM celecoxib	OXAPROZIN	oxaprozin
SODIUM celecoxib celecoxib celecoxib diclofenac potassium diclofenac sodium diclofenac sodium diclofenac sodium diclofenac sodium diclofenac sodium Arthrotec 50 diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium fenoprofen calcium fenoprofen calcium fenoprofen calcium ProFeno	PIROXICAM	
celecoxib celecoxib diclofenac potassium diclofenac sodium diclofenac sodium diclofenac sodium diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium	SUMATRIPTAN SUCCINATE/NAPROXEN	Treximet
celecoxibcelecoxibdiclofenac potassiumCambiadiclofenac potassiumZipsordiclofenac potassiumdiclofenac potassiumdiclofenac sodiumVoltaren-XRdiclofenac sodium/misoprostolArthrotec 50diclofenac sodium/misoprostolArthrotec 75diclofenac sodium/misoprostoldiclofenac-misoprostoldiclofenac submicronizedZorvolexetodolacLodineetodolacetodolacfenoprofen calciumFenorthofenoprofen calciumNalfonfenoprofen calciumProFeno	SODIUM	
diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium diclofenac sodium diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium feroprofen calcium	celecoxib	Celebrex
diclofenac potassium diclofenac potassium diclofenac potassium diclofenac potassium diclofenac sodium Voltaren-XR diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium	celecoxib	celecoxib
diclofenac potassium diclofenac potassium diclofenac sodium diclofenac sodium Voltaren-XR diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium fenoprofen calcium fenoprofen calcium ProFeno	diclofenac potassium	Cambia
diclofenac potassiumdiclofenac potassiumdiclofenac sodiumVoltaren-XRdiclofenac sodium/misoprostolArthrotec 50diclofenac sodium/misoprostolArthrotec 75diclofenac sodium/misoprostoldiclofenac-misoprostoldiclofenac submicronizedZorvolexetodolacLodineetodolacetodolacfenoprofen calciumFenorthofenoprofen calciumNalfonfenoprofen calciumProFeno		Cataflam
diclofenac sodium diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac sodium/misoprostol diclofenac submicronized etodolac etodolac etodolac fenoprofen calcium fenoprofen calcium fenoprofen calcium Fenortho Nalfon fenoprofen calcium ProFeno	diclofenac potassium	Zipsor
diclofenac sodium/misoprostolArthrotec 50diclofenac sodium/misoprostolArthrotec 75diclofenac sodium/misoprostoldiclofenac-misoprostoldiclofenac submicronizedZorvolexetodolacLodineetodolacetodolacfenoprofen calciumFenorthofenoprofen calciumNalfonfenoprofen calciumProFeno	diclofenac potassium	diclofenac potassium
diclofenac sodium/misoprostolArthrotec 75diclofenac sodium/misoprostoldiclofenac-misoprostoldiclofenac submicronizedZorvolexetodolacLodineetodolacetodolacfenoprofen calciumFenorthofenoprofen calciumNalfonfenoprofen calciumProFeno	diclofenac sodium	Voltaren-XR
diclofenac sodium/misoprostoldiclofenac-misoprostoldiclofenac submicronizedZorvolexetodolacLodineetodolacetodolacfenoprofen calciumFenorthofenoprofen calciumNalfonfenoprofen calciumProFeno	diclofenac sodium/misoprostol	Arthrotec 50
diclofenac submicronized etodolac etodolac fenoprofen calcium	diclofenac sodium/misoprostol	Arthrotec 75
etodolac Lodine etodolac etodolac fenoprofen calcium Fenortho fenoprofen calcium Nalfon fenoprofen calcium ProFeno	diclofenac sodium/misoprostol	diclofenac-misoprostol
etodolac etodolac fenoprofen calcium Fenortho fenoprofen calcium Nalfon fenoprofen calcium ProFeno	diclofenac submicronized	Zorvolex
fenoprofen calcium fenoprofen calcium Nalfon fenoprofen calcium ProFeno	etodolac	Lodine
fenoprofen calcium Nalfon fenoprofen calcium ProFeno	etodolac	etodolac
fenoprofen calcium ProFeno	•	
	•	Nalfon
fenoprofen calcium fenoprofen		
	fenoprofen calcium	fenoprofen

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

Generic Name	Brand Name
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
ibuprofen	Infants ProfeniB
ibuprofen	Motrin IB
ibuprofen	Provil
ibuprofen/diphenhydramine HCl	Advil PM Liqui-Gels
ibuprofen/diphenhydramine rici	Advil PM
ibuprofen/diphenhydramine citrate	Motrin PM
ibuprofen/diphenhydramine citrate	
ibuprofen/famotidine	ibuprofen-diphenhydramine cit Duexis
indomethacin	Indocin
indomethacin	indocin
indomethacin, submicronized ketoprofen	Tivorbex ketoprofen
ketorolac tromethamine	ketorolac
meclofenamate sodium	meclofenamate
mefenamic acid	Ponstel
mefenamic acid	mefenamic acid
meloxicam	Qmiiz ODT
meloxicam, submicronized	Vivlodex
nabumetone	nabumetone
naproxen	EC-Naproven
naproxen	EC-Naprosen
naproxen	Naprosyn Aleve
naproxen sodium naproxen sodium	Anaprox
•	•
naproven sodium	Anaprox DS Modiarayan
naproven sodium	Mediproxen Naprelan CR
naproven sodium	Aleve PM
naproxen sodium/diphenhydramine HCl naproxen/esomeprazole magnesium	Vimovo
- · · · · · · · - · · - · · · · · · · ·	
oxaprozin	Daypro
oxaprozin	oxaprozin Foldono
piroxicam	Feldene
piroxicam	piroxicam
sulindac tolmotin sodium	sulindac
tolmetin sodium Diuretics (thiazides, potassium	tolmetin

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Generic Name	Brand Name
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
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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This request executed the Cohort Identification and Descriptive Analysis (CIDA) and Propensity Score Analysis (PSA) tools v11.2.3 with additional programming to assess the risk for angioedema associated with various sacubitril/valsartan (SV) new user subgroups among heart failure patients in the Sentinel Distributed Database (SDD).

Query Period: 7/7/2015 - DP-specific data completeness end date at time of execution of cder_mpl2r_wp016 and cder_mpl2p_wp021

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, KM curves (zoomed in, at-risk table shown)

Data Partners: AEOS, CMS, HCOS, HUOS, OPOS

Freeze Data: On

Additional Programming Needed: Local reporting for KM curves by subgroup and stratified analyses by user-specified risk window

	Compa	arison 1	Compa	Comparison 2		Comparison 3	
	ACEI-SV	ARB-SV	ACEI-SV	SV	ARB-SV	sv	
Drug/Exposure							
Request Package Group	SV_ARB	SV_ACEI	SV_ARB	SV_ACEI_ARB	SV_ACEI	SV_ACEI_ARB	
Exposure/Comparator	SV	SV	SV	SV	SV	SV	
Incident with Respect to:	SV, ARB	SV, ACEI	SV, ARB	SV, ACEI, ARB	SV, ACEI	SV, ACEI, ARB	
Incidence Assessment	Dispensing date	e or days supply	Dispensing date	or days supply	Dispensing date	e or days supply	
Washout (days)	183		183		183		
Cohort Definition	First valid incident	exposure episode	First valid incident	exposure episode	First valid incident	exposure episode	
Stockpiling overlapping claims	Def	ault	Default		Def	ault	
Episode Gap (days)	14		1	4	1	.4	
Episode Extension Period (days)	14		14		14		
Maximum Episode Duration (days)	365		365		365		
Censor Criteria	occurrence, disenrollme	reatment, outcome nt, recorded death, data date	ACEI, ARB, end of to occurrence, disenrollme end		occurrence, disenrollme	reatment, outcome nt, recorded death, data date	

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Appendix H: Specifications Defini		rison 1	Compa	arison 2	Compa	rison 3
	ACEI-SV	ARB-SV	ACEI-SV	SV	ARB-SV	SV
Inclusion/Exclusion*	7102.70	71112 01	7102.70		7.11.2 37	
Pre-Existing Condition	Heart	failure	Heart	failure	Heart	failure
Include/Exclude		ude		ude		ude
Lookback Period (days)	-	3, 0		3, 0	-18	
Pre-Existing Condition	ACEI	ARB	ACEI		ARB	
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	Dispensing date or	Dispensing date or		Dispensing date or	
 	days supply	days supply	days supply		days supply	
Pre-Existing Condition		, ARB		, ARB	ACEI,	ARB
Include/Exclude	Exc	ude	Excl	lude	Excl	ude
Care Setting/PDX	A	ny	Aı	ny	Aı	ny
Lookback Period (days))	0		0	
Inclusion Assessment	Dispensing date		Dispensing date		Dispensing date	
Event/Outcome						
Event/Outcome	Angio	edema	Angio	edema	Angioedema	
Care Setting/PDX	Inpatient, emergency de	epartment or outpatient	Inpatient, emergency de	epartment or outpatient	Inpatient, emergency de	epartment or outpatient
Washout (days))	0		()
Blackout Period (days))	0		()
Propensity Score Matching						
Covariates	See Ap	pendix I	See Appendix I		See Appendix I	
Matching Ratio	1	:1	1:1		1:1	
Matching Caliper Settings	0.	05	0.05		0.05	
Analysis Type	Conditional and	d unconditional	Conditional and unconditional		Conditional and unconditional	
Risk Window Analysis	0-30, 31-60, 61-90, 91-	180, 181-270, 271-365	0-30, 31-60, 61-90, 91-	-180, 181-270, 271-365	0-30, 31-60, 61-90, 91-180, 181-270, 271-365	
Subgroup Analyses						
Stratifying variable	Angio	edema	Angio	edema	Angio	edema
Evaluation Window (days)	-183	3, -1	-183, -1		-183, -1	
Re-matching	Re-matching should	oe done with the pre-	Re-matching should l	be done with the pre-	Re-matching should b	oe done with the pre-
	matche	d cohort	matched cohort		matched	d cohort
Priority output	Y	es	Y	es	Ye	es
Risk Window Analysis (days)		180, 181-270, 271-365	0-30, 31-60, 61-90, 91-180, 181-270, 271-365			180, 181-270, 271-365
Stratifying variable		edema		edema	Angio	
Evaluation Window (days)	_	ment history, -1	_	lment history, -1	Pre-index enrollment history, -1	

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	Compa	rison 1	Compa	rison 2	Compa	arison 3	
	ACEI-SV	ARB-SV	ACEI-SV	SV	ARB-SV	SV	
Re-matching	Re-matching should I	be done with the pre-	Re-matching should l	be done with the pre-	Re-matching should	be done with the pre-	
	matche	d cohort	matche	d cohort	matche	d cohort	
Priority output	N	0	N	lo	N	lo	
Stratifying variable	Serious	allergies	Serious	allergies	Serious	allergies	
Evaluation Window (days)	-183	3, -1	-183	3, -1	-183	3, -1	
Re-matching	Re-matching should I	oe done with the pre-	Re-matching should b	be done with the pre-	Re-matching should	be done with the pre-	
	matche	d cohort	matche	d cohort	matche	d cohort	
Priority output	No		N	lo	N	lo	
Stratifying variable	Age group		Age g	Age group		Age group	
Re-matching	Re-matching should I	oe done with the pre-	Re-matching should be done with the pre-		Re-matching should be done with the pre-		
	matched cohort		matched cohort		matched cohort		
Priority output	N	0	No		No		
Stratifying variable	Se	ex	Sex		S	ex	
Re-matching	Re-matching should I	oe done with the pre-	Re-matching should I	be done with the pre-	Re-matching should be done with the p		
	matche	d cohort	matched cohort		matched cohort		
Priority output	N	0	N	lo	N	lo	
Stratifying variable	Ra	ce	Ra	ice	Ra	ice	
Re-matching	Re-matching should I	oe done with the pre-	Re-matching should b	be done with the pre-	Re-matching should	be done with the pre-	
	matche	d cohort	matche	d cohort	matche	d cohort	
Priority output	Y	es	Yes		Y	es	
Risk Window Analysis (days)	0-30, 31-60, 61-90, 91-	0-30, 31-60, 61-90, 91-180, 181-270, 271-365		-180, 181-270, 271-365	0-30, 31-60, 61-90, 91-	-180, 181-270, 271-365	

International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Edition, Clinical Modification (ICD-10-CM),
Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology, Fourth Edition (CPT-4) 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	ng Parameters for this I	Request	T				
	Compa	rison 4	Compa	Comparison 5		Comparison 6	
	ACEI-SV	ARB-SV	ACEI-SV	SV	ARB-SV	SV	
Drug/Exposure							
Request Package Group	SV_ARB_14	SV_ACEI_14	SV_ARB_14	SV_ACEI_ARB	SV_ACEI_14	SV_ACEI_ARB	
Exposure/Comparator	SV	SV	SV	SV	SV	SV	
Incident with Respect to:	SV, ARB	SV, ACEI	SV, ARB	SV, ACEI, ARB	SV, ACEI	SV, ACEI, ARB	
Incidence Assessment	Dispensing date	or days supply	Dispensing date	or days supply	Dispensing date	e or days supply	
Washout (days)	18	33	18	83	18	83	
Cohort Definition	First valid incident	exposure episode	First valid incident	exposure episode	First valid incident	exposure episode	
Stockpiling overlapping claims	Def	ault	Def	ault	Def	ault	
Episode Gap (days)	1	4	1	.4	1	.4	
Episode Extension Period (days)	1	4	1	.4	1	.4	
Maximum Episode Duration (days)	30	55	365		365		
Censor Criteria	occurrence, disenrollme	EI, ARB, end of treatment, outcome and disease and date ACEI, ARB, end of treatment occurrence, disease and date		nt, recorded death, data	ACEI, ARB, end of treatment, outcome occurrence, disenrollment, recorded death, data end date		
Inclusion/Exclusion* Pre-Existing Condition Include/Exclude	Incl	failure ude	Heart failure Include		Incl	failure lude	
Lookback Period (days)		3, 0		-183, 0 -183, 0		I	
Pre-Existing Condition Include/Exclude Care Setting/PDX Lookback Period (days) Inclusion Assessment	ACEI Include Any -14, 0 Dispensing date or days supply	ARB Include Any -14, 0 Dispensing date or days supply	ACEI Include Any -14, 0 Dispensing date or days supply	 	ARB Include Any -14, 0 Dispensing date or days supply	 	
Pre-Existing Condition Include/Exclude Care Setting/PDX Lookback Period (days) Inclusion Assessment	ACEI, ARB Exclude Any 0 Dispensing date		ACEI, ARB Exclude Any 0 Dispensing date		ACEI, ARB Exclude Any 0 Dispensing date		
Event/Outcome Event/Outcome	Angio	edema	Angio	edema	Angio	edema	

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	Compa	rison 4	Compa	rison 5	Comp	arison 6
	ACEI-SV	ARB-SV	ACEI-SV	SV	ARB-SV	SV
Care Setting/PDX	Inpatient, emergency department or outpatient		Inpatient, emergency de	epartment or outpatient	Inpatient, emergency d	epartment or outpatient
Washout (days))	()		0
Blackout Period (days))	()		0
Propensity Score Matching						
Covariates	See App	oendix I	See App	oendix I	See Ap	pendix I
Matching Ratio	1	1	1:	:1	:	1:1
Matching Caliper Settings	0.	05	0.0	05	0	.05
Analysis Type	Conditional and	unconditional	Conditional and	d unconditional	Conditional ar	d unconditional
Risk Window Analysis	0-30, 31-60, 61-90, 91-	180, 181-270, 271-365	0-30, 31-60, 61-90, 91-	180, 181-270, 271-365	0-30, 31-60, 61-90, 91	-180, 181-270, 271-365
Subgroup Analyses						
Stratifying variable	Angioedema		Angioedema		Angioedema	
Evaluation Window (days)	-183	3, -1	-183, -1		-183, -1	
Re-matching	Re-matching should b	e done with the pre-	Re-matching should be done with the pre-		Re-matching should be done with the pre-	
Priority output	Ye	 es	Yes		Yes	
Risk Window Analysis (days)	0-30, 31-60, 61-90, 91-	180, 181-270, 271-365	0-30, 31-60, 61-90, 91-180, 181-270, 271-365		0-30, 31-60, 61-90, 91	-180, 181-270, 271-365
Stratifying variable	Angio	edema	Angioedema		Angioedema	
Evaluation Window (days)	Pre-index enroll	ment history, -1	Pre-index enrollment history, -1		Pre-index enrollment history, -1	
Re-matching	Re-matching should be		Re-matching should be done with the pre-		Re-matching should be done with the pre-	
Priority output	matched N		matched N	d cohort o		ed cohort No
Stratifying variable	Serious	allergies	Serious	allergies	Serious	allergies
Evaluation Window (days)	-183	3, -1	-183, -1		-183, -1	
Re-matching	Re-matching should b	e done with the pre-	Re-matching should b	oe done with the pre-	Re-matching should	be done with the pre-
		matched cohort		matched cohort		ed cohort
Priority output	N		No			No
Stratifying variable Re-matching	.	Age group Re-matching should be done with the pre-		Age group Re-matching should be done with the pre-		group be done with the pre-
ve-matching	matched	· ·	_	d cohort	_	ed cohort
Priority output	N			0		No

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	Compa	rison 4	Compa	Comparison 5		Comparison 6	
	ACEI-SV	ARB-SV	ACEI-SV	sv	ARB-SV	SV	
Stratifying variable	S	ex	Se	ex	Se	ex	
Re-matching	Re-matching should I	oe done with the pre-	Re-matching should b	e done with the pre-	Re-matching should I	be done with the pre-	
	matche	d cohort	matched	d cohort	matche	d cohort	
Priority output	No		No		No		
Stratifying variable	Ra	ice	Race		Race		
Re-matching	Re-matching should I	oe done with the pre-	Re-matching should be done with the pre-		Re-matching should be done with the pre-		
	matche	d cohort	matched cohort		matched cohort		
Priority output	Y	es	Yes Yes		es		
Risk Window Analysis (days)	0-30, 31-60, 61-90, 91-	180, 181-270, 271-365	0-30, 31-60, 61-90, 91-180, 181-270, 271-365		0-30, 31-60, 61-90, 91-180, 181-270, 271-365		

International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Edition, Clinical Modification (ICD-10-CM),
Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology, Fourth Edition (CPT-4) 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 Baseline Characterstics and Propensity Score Analysis Covariates Evaluated in this Request

Request	KEY: Highlighted = Characteristic not
Baseline Covariate Groups Evaluated in this Request	included in Propensity-Score Model
Covariate	Covariate Evaluation Window
age (continuous)	Index date
ge-group	
18-44	Index date
45-54	Index date
55-64	Index date
65+	Index date
ex	
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
lispanic Ethnicity	Index date
'ear	
2015	Index date
2016	Index date
2017	Index date
2018	Index date
2019	Index date
2020	Index date
Combined comorbidity score	-183 to 0
ngioedema	-183 to -1
angioedema	Ever to -1
mbulatory allergies (AV/OA) or allergy treatment	-183 to -1
erious allergies (ED/IP)	-183 to -1
mbulatory allergies or treatment and not serious allergies	-183 to -1
liabetes	-183 to 0
chemic heart disease	-183 to 0
enal disorders	-183 to 0
viuretics (thiazides, potassium sparing, loop diuretics)	-183 to 0
Ionsteroidal anti-inflammatory drugs (NSAIDs)	-183 to 0
irolimus	-183 to 0
verolimus ealth care utilization	-183 to 0
	192 + 0.0
lumber of inpatient hospital stays	-183 to 0
umber of emergency department visits	-183 to 0
lumber of institutional stay visits	-183 to 0 -183 to 0
Number of ambulatory visits	
Jumber of other ambulatory visits Orug utilization	-183 to 0
Nean number of filled prescriptions	-183 to 0
Mean number of fined prescriptions	-183 to 0
Mean number of unique drug classes	-183 to 0
real number of unique drug classes	-103 (0 0

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