Disclaimer

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_mpl1p_wp023

Request ID: cder_mpl1p_wp023_nsdp_v01

Request Description: This report contains estimates of hydrochlorothiazide (HCTZ), angiotensin-converting enzyme inhibitor (ACEI), and angiotensin II receptor blocker (ARB) utilization in the Sentinel Distributed Database (SDD).

Sentinel Modular Program Tool Used: Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.3 with additional ad hoc programming.

Data Source: Data from January 1, 2000 to June 30, 2018 from 17 Data Partners contributing to the SDD were included in this report. This request was distributed to Data Partners on August 20, 2018. Please see Appendix A for dates of available data for each Data Partner.

Study Design: The request was designed to calculate length and dose of cumulative treatment episodes and enrolled time. Results were stratified by race and enrolled follow-up time.

Exposures of Interest: The exposures of interest were any HCTZ-containing product (including HCTZ monotherapy, HCTZ-ACEI combination products, HCTZ-ARB combination products, and HCTZ-amiloride combination products), ACEI monotherapy, non-HCTZ ACEI combination products, ARB monotherapy, and non-HCTZ ARB combination products. These exposures were identified using National Drug Codes (NDC). See Appendix B for generic drug names used to define the exposures of interest.

Cohort Eligibility Criteria: Members included in the cohort were required to be enrolled in health plans with medical and drug coverage for 183 days prior to the dispensing date of the exposure of interest, during which gaps in enrollment coverage of up to 45 days were allowed. Incidence was assessed in the 183 days prior to the dispensing of interest (index), with respect to the index-defining drugs of interest. The following age groups were analyzed in the cohort: 0-19, 20-44, 45-64, 65+ years.

Dose Calculation: Cumulative exposed time and cumulative dose of a member's exposure to any HCTZ-containing product were calculated from the date of a member's index dispensing to the first occurrence of any of the following: (1) death; (2) end of exposure episode; (3) end of Data Partner data availability; or (4) disenrollment. Only exposure episodes during the first continuous enrollment span contributed to the calculation of cumulative exposure.

All NDC dispensings were stockpiled to sum the days' and amount supply of overlapping dispensings. Additionally, same-day dispensings were summed together. When calculating the length of treatment episodes, a zero-day gap was used. When calculating cumulative dose of HCTZ use, gaps between exposure episodes within a continuous enrollment were allowed.

Dose of each dispensing was calculated by multiplying the amount supplied and the HCTZ strength unique to each NDC. Cumulative dose represented the sum of doses associated with all HCTZ-containing dispensings, including and following the initial index-defining dispensing. For dispensings with amount supplied values outside of the expected range of 1-365 days, the amount supplied value was replaced with the days supplied. Exceptions to this replacement applied to the following custom values: 600, 900, 1800, 6000, 9000, 18000; these raw amount supplied values were replaced with the custom amount supplied values of 60, 90, 180, 60, 90, and 180, respectively.

Please refer to Appendices C and D for detailed specifications of parameters used in this request.

Limitations: Algorithms used to define exposures and dose are imperfect; thus, it is possible that there may be misclassification. Therefore, data should be interpreted with this limitation in mind.

Notes: Please contact the Sentinel Operations Center Query Fulfillment Team (qf@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

Sentinel

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

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). Along with the Principal Diagnosis Indicator, 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).

Cohort Definition (drug/exposure) - indicates how the cohort will be defined: (1): Cohort includes only the first valid treatment episode during the query period; (2): Cohort includes all valid treatment episodes during the query period; (3): Cohort includes all valid treatment episodes during the query period until an event occurs.

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 MP algorithm: (0): Counts all occurrences of an 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 days are added after any episode gaps have been bridged

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

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

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.

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.

*not all terms may be used in this report

Table 1. Summary of New Users of Hydrochlorothiazide (HCTZ), Angiotensin-Converting Enzyme Inhibitors (ACEIs), and Angiotensin II Receptor Blockers (ARBs) in the Sentinel Distributed Database (SDD) between January 1, 2000 to June 30, 2018, by Follow-up Time

	Number of New Users by Length of Enrollment From Index Date							
	0-<1 year	1-<2 years	2-<3 years	3-<4 years	4-<5 years	5-<6 years	6-<7 years	7+ years
Hydrochlorothiazide								
Any HCTZ-Containing Product	2,614,717	1,914,035	1,485,969	1,168,942	973,977	569,553	256,009	906,118
HCTZ Monotherapy	1,600,252	1,175,331	914,504	722,310	627,615	341,156	159,244	573,658
HCTZ-ACEI Combination	717,171	518,542	399,473	313,655	265,005	163,150	87,729	270,351
HCTZ-ARB Combination	593,507	448,077	353,026	274,521	226,777	127,746	51,851	105,806
HCTZ-Amiloride Combination	4,530	3,473	2,815	2,447	2,626	1,271	543	1,370
Angiotensin-Converting Enzyme Inhibitors (ACEIs)								
ACEI Monotherapy	3,092,849	2,221,531	1,688,895	1,327,490	1,059,461	592,935	257,587	823,953
ACEI Combinations (Non-HCTZ)	117,253	90,521	68,962	53,022	46,193	26,706	12,136	34,122
Angiotensin II Receptor Blockers (ARBs)								
ARB Monotherapy	1,629,999	1,180,196	904,491	702,924	560,359	290,235	118,761	292,879
ARB Combinations (Non-HCTZ)	94,403	67,411	55,202	42,694	38,345	22,599	9,190	22,049

Table 2. Summary of New Users of Hydrochlorothiazide (HCTZ), Angiotensin-Converting Enzyme Inhibitors (ACEIs), and Angiotensin II Receptor Blockers (ARBs) in the Sentinel Distributed Database (SDD) between January 1, 2000 to June 30, 2018, by Race

	New Users	Eligible Members[1]	New Users per 10,000 Eligible Members	Eligible Member-Years[1]
Hydrochlorothiazide				
Any HCTZ-Containing Product				
Non-White	1,267,994	9,934,393	1276.37	38,163,635.6
White	4,445,741	41,826,208	1062.91	145,961,988.7
Unknown	4,175,585	112,156,752	372.30	274,780,832
HCTZ Monotherapy				
Non-White	852,134	10,523,935	809.71	42,093,025.4
White	2,955,515	44,390,066	665.81	162,269,790.7
Unknown	2,306,421	114,201,513	201.96	286,514,503
HCTZ-ACEI Combination				
Non-White	370,864	10,683,609	347.13	44,857,829.5
White	1,133,700	45,024,665	251.80	171,756,461.3
Unknown	1,230,512	114,484,969	107.48	290,689,303
HCTZ-ARB Combination				
Non-White	292,194	10,625,715	274.99	45,265,767.4
White	898,283	44,870,265	200.20	172,862,535.1
Unknown	990,834	114,302,602	86.69	290,562,423
HCTZ-Amiloride Combination				
Non-White	1,981	10,844,613	1.83	46,877,011.0
White	9,386	45,749,847	2.05	178,852,089.6
Unknown	7,708	115,098,355	0.67	295,825,654
Angiotensin-Converting Enzyme Inhibitors (ACEIs)				
ACEI Monotherapy				
Non-White	1,280,785	10,074,494	1271.31	39,164,677.3
White	5,544,221	41,183,891	1346.21	142,924,712.6
Unknown	4,239,695	112,550,203	376.69	276,711,622
ACEI Combinations (Non-HCTZ)				
Non-White	64,752	10,784,303	60.04	46,406,256.5
White	157,390	45,520,639	34.58	177,319,104.5
Unknown	226,773	114,850,312	19.75	294,282,012.7
Angiotensin II Receptor Blockers (ARBs)				
ARB Monotherapy				
Non-White	767,305	10,481,955	732.02	43,217,961.4
White	2,913,692	43,940,814	663.09	164,274,699.3
Unknown	1,998,847	113,971,849	175.38	287,364,233.1
ARB Combinations (Non-HCTZ)				
Non-White	49,969	10,826,068	46.16	46,656,990.1
White	124,796	45,704,126	27.31	178,287,954.3
Unknown	177,128	115,053,762	15.40	295,211,189.8

[1]Eligible Members and Member-Years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period

Table 3a. Summary of Cumulative Dose of Hydrochlorothiazide (HCTZ) Among New Users of Any HCTZ-Containing Products, in the Sentinel Distributed Database (SDD) between January 1, 2000 to June 30, 2018, by Follow-up Time

	Length of Enrollment from Index Date (after establishing new use)							
Cumulative Dose	**0-<1 year**	**1-<2 years**	**2-<3 years**	**3-<4 years**	**4-<5 years**	**5-<6 years**	**6-<7 years**	**7+ years**
<10,000mg	2,612,217	1,866,533	1,341,599	967,891	744,524	403,618	167,930	489,574
10,000 - 24,999mg	2,486	46,980	140,333	190,536	205,223	138,588	66,637	232,031
25,000 - 49,999mg	13	515	3,989	10,222	23,271	26,016	20,039	135,075
50,000 - 74,999mg	1	7	46	271	913	1,218	1,184	34,857
75,000 - 99,999mg	0	0	2	21	39	101	208	9,843
>100,000mg	0	0	0	1	7	12	11	4,738

Table 3b. Summary of Cumulative Dose of Hydrochlorothiazide (HCTZ) Among New Users of Any HCTZ-Containing Products, in the Sentinel Distributed Database (SDD) between January 1, 2000 to June 30, 2018, by Follow-up Time and Race

	Length of Enrollment from Index Date (after establishing new use)							
Cumulative Dose	**0-<1 year**	**1-<2 years**	**2-<3 years**	**3-<4 years**	**4-<5 years**	**5-<6 years**	**6-<7 years**	**7+ years**
<10,000mg								
Non-White	290,158	223,970	168,481	125,477	99,224	51,191	18,819	77,516
White	958,645	788,824	644,227	502,207	424,587	216,766	61,247	231,866
Unknown	1,363,414	853,739	528,891	340,207	220,713	135,661	87,864	180,192
10,000 - 24,999mg								
Non-White	290	6,023	19,890	27,932	31,246	20,349	8,968	41,519
White	1,098	20,440	63,219	92,189	109,849	69,974	22,047	102,940
Unknown	1,098	20,517	57,224	70,415	64,128	48,265	35,622	87,572
25,000 - 49,999mg								
Non-White	0	59	528	1,383	3,193	3,821	3,221	30,389
White	5	268	2,069	5,483	13,053	13,042	6,780	65,107
Unknown	8	188	1,392	3,356	7,025	9,153	10,038	39,579
50,000 - 74,999mg								
Non-White	0	1	1	40	129	170	186	9,630
White	0	2	26	164	553	643	482	19,052
Unknown	1	4	19	67	231	405	516	6,175
75,000 - 99,999mg								
Non-White	0	0	1	2	2	14	39	2,806
White	0	0	1	17	25	55	86	5,760
Unknown	0	0	0	2	12	32	83	1,277
>100,000mg								
Non-White	0	0	0	0	0	1	0	1,325
White	0	0	0	1	5	7	4	2,926
Unknown	0	0	0	0	2	4	7	487

Table 4a. Summary of Cumulative Duration of Use of Hydrochlorothiazide (HCTZ) Among New Users of Any HCTZ-Containing Products, in the Sentinel Distributed Database (SDD) between January 1, 2000 to June 30, 2018, by Enrolled Follow-up Time

	Length of Enrollment from Index Date (after establishing new use)							
Cumulative Duration of Use	**0-<1 year**	**1-<2 years**	**2-<3 years**	**3-<4 years**	**4-<5 years**	**5-<6 years**	**6-<7 years**	**7+ years**
0-<1 year	2,614,717	1,203,621	701,468	487,485	373,737	202,512	85,016	240,999
1-<2 years	0	710,414	392,567	209,573	148,918	80,162	32,694	93,933
2-<3 years	0	0	391,934	233,071	131,168	66,153	26,057	70,370
3-<4 years	0	0	0	238,813	159,918	65,487	24,715	66,828
4-<5 years	0	0	0	0	160,236	87,459	24,863	63,019
5-<6 years	0	0	0	0	0	67,780	32,131	59,918
6-<7 years	0	0	0	0	0	0	30,533	69,632
7+ years	0	0	0	0	0	0	0	241,419

Table 4b. Summary of Cumulative Duration of Use of Hydrochlorothiazide (HCTZ) Among New Users of Any HCTZ-Containing Products, in the Sentinel Distributed Database (SDD) between January 1, 2000 to June 30, 2018, by Enrolled Follow-up Time and Race

	Length of Enrollment from Index Date (after establishing new use)							
Cumulative Duration of Use	**0-<1 year**	**1-<2 years**	**2-<3 years**	**3-<4 years**	**4-<5 years**	**5-<6 years**	**6-<7 years**	**7+ years**
0-<1 year								
Non-White	290,448	154,037	95,112	67,609	53,268	27,515	10,129	40,177
White	959,748	478,762	320,237	243,581	206,493	103,861	28,605	105,305
Unknown	1,364,521	570,822	286,119	176,295	113,976	71,136	46,282	95,517
1-<2 years								
Non-White	0	76,016	53,586	32,348	23,933	12,317	4,470	17,891
White	0	330,772	177,999	100,469	78,880	40,681	10,877	40,445
Unknown	0	303,626	160,982	76,756	46,105	27,164	17,347	35,597
2-<3 years								
Non-White	0	0	40,203	30,325	19,777	9,812	3,359	12,935
White	0	0	211,306	117,346	70,749	33,461	8,583	29,730
Unknown	0	0	140,425	85,400	40,642	22,880	14,115	27,705
3-<4 years								
Non-White	0	0	0	24,552	20,350	8,980	3,336	12,564
White	0	0	0	138,665	90,747	34,456	8,125	29,036
Unknown	0	0	0	75,596	48,821	22,051	13,254	25,228
4-<5 years								
Non-White	0	0	0	0	16,466	10,171	3,108	11,730
White	0	0	0	0	101,203	49,420	8,637	27,686
Unknown	0	0	0	0	42,567	27,868	13,118	23,603
5-<6 years								
Non-White	0	0	0	0	0	6,751	3,672	10,643
White	0	0	0	0	0	38,608	11,962	26,022
Unknown	0	0	0	0	0	22,421	16,497	23,253
6-<7 years								
Non-White	0	0	0	0	0	0	3,159	11,776
White	0	0	0	0	0	0	13,857	31,759
Unknown	0	0	0	0	0	0	13,517	26,097
7+ years								
Non-White	0	0	0	0	0	0	0	45,469
White	0	0	0	0	0	0	0	137,668
Unknown	0	0	0	0	0	0	0	58,282

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (August 20, 2018)

Data Partner ID	Start Date[1]	End Date[1]
DP01	06/01/2007	10/31/2017
DP02	01/01/2000	10/31/2017
DP03	01/01/2000	06/30/2018
DP04	01/01/2008	03/31/2018
DP05	01/01/2006	12/31/2017
DP06	01/01/2000	12/31/2016
DP07	01/01/2008	06/30/2017
DP08	01/01/2010	12/31/2015
DP09	01/01/2005	09/30/2017
DP10	01/01/2000	03/31/2016
DP11	01/01/2000	05/31/2015
DP12	01/01/2000	03/31/2018
DP13	01/01/2000	12/31/2017
DP14	01/01/2000	06/30/2017
DP15	01/01/2004	01/31/2018
DP16	01/01/2000	03/31/2018
DP17	01/01/2012	06/30/2017

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

Appendix B. List of Generic Drug Names Used to Define Exposures in this Request

Generic Name
Any Hydrochlorothiaizde (HCTZ)-Containing Product
benazepril HCl/hydrochlorothiazide
captopril/hydrochlorothiazide
enalapril maleate/hydrochlorothiazide
fosinopril sodium/hydrochlorothiazide
lisinopril/hydrochlorothiazide
moexipril HCl/hydrochlorothiazide
quinapril HCl/hydrochlorothiazide
amiloride HCl/hydrochlorothiazide
amlodipine besylate/valsartan/hydrochlorothiazide
candesartan cilexetil/hydrochlorothiazide
eprosartan mesylate/hydrochlorothiazide
irbesartan/hydrochlorothiazide
losartan potassium/hydrochlorothiazide
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide
olmesartan medoxomil/hydrochlorothiazide
telmisartan/hydrochlorothiazide
valsartan/hydrochlorothiazide
hydrochlorothiazide
aliskiren hemifumarate/amlodipine/hydrochlorothiazide
aliskiren hemifumarate/hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide
guanethidine sulfate/hydrochlorothiazide
hydralazine HCl/hydrochlorothiazide
hydralazine HCl/reserpine/hydrochlorothiazide
methyldopa/hydrochlorothiazide
metoprolol succinate/hydrochlorothiazide
metoprolol tartrate/hydrochlorothiazide
propranolol HCl/hydrochlorothiazide
reserpine/hydrochlorothiazide
spironolactone/hydrochlorothiazide
timolol maleate/hydrochlorothiazide
triamterene/hydrochlorothiazide
HCTZ Monotherapy
hydrochlorothiazide
Angiotensin-Converting Enzyme Inhibitors (ACEI) - HCTZ Combination Products
benazepril HCl/hydrochlorothiazide
captopril/hydrochlorothiazide
enalapril maleate/hydrochlorothiazide
fosinopril sodium/hydrochlorothiazide
lisinopril/hydrochlorothiazide
moexipril HCl/hydrochlorothiazide
quinapril HCl/hydrochlorothiazide
Angiotensin II Receptor Blockers (ARB) - HCTZ Combination Products
amlodipine besylate/valsartan/hydrochlorothiazide
candesartan cilexetil/hydrochlorothiazide
eprosartan mesylate/hydrochlorothiazide
irbesartan/hydrochlorothiazide
losartan potassium/hydrochlorothiazide
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide
olmesartan medoxomil/hydrochlorothiazide
telmisartan/hydrochlorothiazide
valsartan/hydrochlorothiazide
Amiloride - HCTZ Combination Products

Appendix B. List of Generic Drug Names Used to Define Exposures in this Request

Generic Name
amiloride HCl/hydrochlorothiazide
ACEI Monotherapy
benazepril HCl
captopril
enalapril maleate
fosinopril sodium
lisinopril
moexipril HCl
perindopril erbumine
quinapril HCl
ramipril
trandolapril
Non-HCTZ ACEI Combination Products
amlodipine besylate/benazepril HCl
enalapril maleate/diltiazem malate
enalapril maleate/felodipine
lisinopril/dietary supplement,comb.10
perindopril arginine/amlodipine besylate
trandolapril/verapamil HCl
ARB Monotherapy
azilsartan medoxomil
candesartan cilexetil
eprosartan mesylate
irbesartan
losartan potassium
olmesartan medoxomil
telmisartan
valsartan
Non-HCTZ ARB Combination Products
amlodipine besylate/olmesartan medoxomil
amlodipine besylate/valsartan
azilsartan medoxomil/chlorthalidone
nebivolol HCl/valsartan
sacubitril/valsartan
telmisartan/amlodipine besylate

Appendix C. Specifications for Parameters for Request cder_mpl1p_wp023

This request uses the Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.3, to calculate utilization hydrochlorothiaizde (HCTZ), chlorothiazide (CTZ), bendroflumethiazide (BFMTZ), angiotensin-converting enzyme inhibitors (ACEI), beta blockers, or calcium channel blockers (CaChannel) in the Sentinel Distributed Database (SDD).

Query Period: January 1, 2000 - August 20, 2018
Enrollment Requirement: 183 days
Enrollment Gap: 45 days
Coverage Requirement: Medical and Drug
Age Stratifications: 0-19, 20-44, 45-64, 65+ years
Results Stratified by: Race

	Exposure					
Scenario	**Exposure**	**Incident with Respect to:**	**Washout (days)**	**Censor**	**Censor Categories (years)**	**Cohort Definition**
1	Any HCTZ products, all product stockpiling	Any HCTZ products	183	Death, Data Partner (DP) End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
2	HCTZ monotherapy	HCTZ monotherapy	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
3	HCTZ-ACEI combination	HCTZ-ACEI combination	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
4	HCTZ-ARBs combination	HCTZ-ARBs combination	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
5	HCTZ-amiloride combination	HCTZ-amiloride combination	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
6	ACEI monotherapy	ACEI monotherapy	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
7	ACEI combinations (non-HCTZ combinations)	ACEI combinations (non-HCTZ combinations)	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
8	ARB monotherapy	ARB monotherapy	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures
9	ARB combinations (non-HCTZ combinations)	ARB combinations (non-HCTZ combinations)	183	Death, DP End Date	0<1, 1<2, 2<3, 3<4, 4<5, 5<6, 6<7, and 7+	01: First valid incident exposures

National Drug Codes (NDCs) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

Appendix D. Specifications for Parameters for Request cder_mpl1p_wp023, Dose Calculation

This request uses the Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.4 to calculate rates of non-melanoma skin cancer (NMSC) events after exposure to hydrochlorothiaizde (HCTZ), chlorothiazide (CTZ), bendroflumethiazide (BFMTZ), angiotensin-converting enzyme inhibitors (ACEI), beta blockers, or calcium channel blockers (CaChannel) in the Sentinel Distributed Database (SDD).

Query Period: January 1, 2000 - August 20, 2018
Enrollment Requirement: 183 days
Enrollment Gap: 45 days
Coverage Requirement: Medical and Drug
Age Stratifications: 0-19, 20-44, 45-64, 65+ years

	Exposure				Episode Creation				
Scenario	**Exposure**	**Incident with Respect to:**	**Washout (days) - For first Dispensings**	**Censor**	**Episode Gap**	**Stockgroup Criteria**	**Same-Day Dispensings**	**Days Supplied Range**	**Amount Supplied Range ***
10	Any HCTZ products, all product stockpiling	Any HCTZ products, all product stockpiling	183	Death, Data Partner End Date	Fixed, 0 days	All NDCs same stockgroup	Sum (keep all)	Any	1-365

National Drug Codes (NDCs) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

*For amount supply outside of the expected range of 1-365, amount supplied will be replaced with days supply of the claim - except for the following values:

Raw Amount Supplied	Custom Amount Supplied
600	60
900	90
1800	180
6000	60
9000	90
18000	180