



Modular Program Report

The following report(s) provides findings from an FDA-initiated query using its Mini-Sentinel pilot. While Mini-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 Mini-Sentinel, and seeking to better understand the capabilities of the Mini-Sentinel pilot.

Data obtained through Mini-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 the Mini-Sentinel pilot in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Mini-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	
<u>Request Description</u>	<p>FDA requested execution of Modular Program #3 (MP3), version 4.0, to investigate use of several anti-epileptic drug products (AEDs) and diagnosis of kidney stones (See Appendix A). Due to the large list of exposure codes, a code list for AEDs is not provided in this report. Please contact the Mini-Sentinel Operations Center (MSOC_Requests@harvardpilgrim.org) for a list of exposure codes. Each product was analyzed by two unique incidence definitions and two unique kidney stone definitions. Incidence was defined with respect to a specified list of AEDs as well as with respect to the drug of interest, acetazolamide, topiramate, and zonisamide only. Kidney stone events were defined with the list of codes in Appendix A: one definition including ICD-9-CM diagnosis code 788.0, the other excluding ICD-9-CM diagnosis code 788.0. The query was run against the Mini-Sentinel Distributed Database (MSDD) for the time period of January 1, 2004 to December 31, 2012. This request was distributed to 18 Mini-Sentinel Data Partners on April 26, 2013.</p> <p>This report presents results for lamotrigine, levetiracetam, and topiramate only. Separate reports present results for carbamazepine, oxcarbazepine, and zonisamide (MSY4_MPR29_V1, Report 2 of 3) and gabapentin and phenytoin (MSY4_MPR29_V1, Report 3 of 3).</p> <p>Results provide counts of new AED users, total dispensings, new episodes, days supplied, days at risk (days supplied + any episode gap days + any episode extension days), kidney stone events, eligible members, and member-days.</p>
<u>Request ID</u>	msy4_mpr29_v1 Report 1 of 3

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<u>Notes:</u>	Please contact the Mini-Sentinel Operations Center (MSOC_Requests@harvardpilgrim.org) for questions and to provide comments/suggestions for future enhancements to this document

Modular Program Specifications MSY4_MPR29_V1

Modular Program #3, version 4.0, was used to investigate exposure to antiepileptic drugs (AEDs) and kidney stone events. The query period was from January 1, 2004 to December 31, 2012, and the enrollment gap was set at 45 days. Age groups were split as follows: 0-<2, 2-<5, 5-<10, 10-<17, 17-<40, 40-<65, 65+ years. In total, 12 different scenarios with differing exposures of interest, incidence definitions, and event definitions were examined in this report.

Drug/Exposure									Event/Outcome								
Incident exposure	Incident w/ respect to:	Washout (days)	Incidence Type	Episode Gap	Exposure Extension Period	Min. Episode Duration	Min. Days Supplied	Event/ Outcome	Care Setting	Principal Dx	Event incident w/ respect to:	Incident Only Care Setting	Washout (days)	Incidence Type	Incident Only Principal Dx	Blackout Period	
IVIG																	
1	topiramate	All AEDs	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
2	topiramate	All AEDs	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
3	topiramate	topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
4	topiramate	topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
5	lamotrigine	All AEDs	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
6	lamotrigine	All AEDs	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
7	lamotrigine	lamotrigine, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0

Modular Program Specifications MSY4_MPR29_V1

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Drug/Exposure									Event/Outcome								
Incident exposure	Incident w/ respect to:	Washout (days)	Incidence Type	Episode Gap	Exposure Extension Period	Min. Episode Duration	Min. Days Supplied	Event/ Outcome	Care Setting	Principal Dx	Event incident w/ respect to:	Incident Only Care Setting	Washout (days)	Incidence Type	Incident Only Principal Dx	Blackout Period	
8	lamotrigine	lamotrigine, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
9	levetiracetam	All AEDs	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
10	levetiracetam	All AEDs	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
11	levetiracetam	levetiracetam, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
12	levetiracetam	levetiracetam, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0

NDC codes checked against First Data Bank's "National Drug Data File (NDDF®) Plus"
 ICD-9-CM diagnosis and procedure codes checked against "Ingenix 2012 ICD-9-CM Data File" provided by OptumInsight
 HCPCS codes checked against "Optum 2012 HCPCS Level II Data File" provided by OptumInsight
 CPT codes checked against "Optum 2012 Current Procedure Codes & Relative Values Data File" provided by OptumInsight

Glossary of Terms in Modular Program 3*

- 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).
- Days at Risk** - number of days supplied plus any episode gaps and exposure extension periods.
- 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.
- Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.
- Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.
- Incidence Type (drug/exposure)**- *Minimum incidence type* will consider the first treatment episode in the query period as long as it is the first treatment episode in the user's entire available history. *Single* and *Multiple incidence types* will use the washout period to establish incidence, however *Single* will only consider the first treatment episode whereas *Multiple* will consider all qualifying incident treatment episodes.
- Incidence Type (event/outcome)**- *Minimum incidence type* considers the first event in a valid episode as long as it is the first event in the user's entire available history. *Multiple incidence type* uses the washout period to establish incidence and considers all qualifying incident treatment episodes. The program will only consider one event per episode, but the *Multiple incidence type* will consider more than one event per user if a user has more than one incident episode.
- Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).
- Member-Days** - sum of all days of enrollment with medical and drug coverage** in the query period preceded by an exposure washout period.
- 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.
- New Episodes** - new treatment episodes; length of episode is determined by days supplied in one dispensing (or consecutive dispensings bridged by the episode gap).
- New Users** - number of members with incident exposure during the query period. Member must have no evidence of exposure (s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.
- Principal Diagnosis** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. YES will only consider diagnoses flagged as Principal.
- Query Period** - period in which the modular program looks for exposures and outcomes of interest.
- Total Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.
- 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.

*all terms may not be used in this report

**incident treatment episodes must be incident to both the exposure and the event

Table 1: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, and Kidney Stone (Events) Definition

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Lamotrigine													
Incident to All AEDs													
Events including code 788	189,318	189,318	688,870	23,452,586	24,303,873	897	91,178,386	74,988,435,916	2.08	123.88	3.64	34.05	3.69
Events excluding code 788	189,473	189,473	689,287	23,466,321	24,327,684	820	91,183,218	75,016,339,985	2.08	123.85	3.64	34.04	3.37
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788	309,961	309,961	1,337,240	46,567,136	48,272,175	2,018	92,737,218	78,321,329,337	3.34	150.24	4.31	34.82	4.18
Events excluding code 788	310,273	310,273	1,338,312	46,601,241	48,345,780	1,829	92,741,941	78,352,630,727	3.35	150.19	4.31	34.82	3.78
Levetiracetam													
Incident to All AEDs													
Events including code 788	83,419	83,419	307,578	10,565,308	10,692,147	430	91,178,405	75,015,778,652	0.91	126.65	3.69	34.35	4.02
Events excluding code 788	83,492	83,492	307,867	10,574,783	10,705,131	400	91,183,237	75,043,725,376	0.92	126.66	3.69	34.35	3.74
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788	145,373	145,373	668,746	23,593,437	24,137,875	1,023	92,853,029	78,533,478,666	1.57	162.30	4.60	35.28	4.24
Events excluding code 788	145,520	145,520	669,258	23,610,689	24,168,674	949	92,857,758	78,565,015,507	1.57	162.25	4.60	35.28	3.93
Topiramate													
Incident to All AEDs													
Events including code 788	347,867	347,867	873,098	29,792,150	31,975,167	2,261	91,178,369	74,926,494,251	3.82	85.64	2.51	34.12	7.07
Events excluding code 788	348,198	348,198	873,843	29,815,959	32,023,732	2,083	91,183,201	74,954,261,554	3.82	85.63	2.51	34.12	6.50
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788	497,786	497,786	1,430,976	49,443,984	52,978,571	3,945	92,909,350	78,489,396,407	5.36	99.33	2.87	34.55	7.45
Events excluding code 788	498,312	498,312	1,432,360	49,489,499	53,077,169	3,621	92,914,079	78,520,686,583	5.36	99.31	2.87	34.55	6.82

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Lamotrigine													
Incident to All AEDs													
Events including code 788													
00 to 01 year	76	76	182	6,231	6,404	0	3,797,546	1,270,229,122	0.02	81.99	2.39	34.24	0.00
02 to 04 years	575	575	2,217	76,430	78,169	1	5,799,340	2,878,396,116	0.10	132.92	3.86	34.47	1.28
05 to 09 years	4,082	4,082	19,455	625,704	650,447	3	8,390,498	5,107,481,914	0.49	153.28	4.77	32.16	0.46
10 to 16 years	21,116	21,116	89,176	2,865,506	3,011,420	29	11,197,442	7,714,305,052	1.89	135.70	4.22	32.13	0.96
17 to 39 years	94,165	94,165	307,452	10,084,250	10,574,385	432	35,685,167	23,039,382,097	2.64	107.09	3.27	32.80	4.09
40 to 64 years	63,339	63,339	247,300	8,879,067	9,063,784	385	33,173,782	27,535,646,395	1.91	140.18	3.90	35.90	4.25
65+ years	5,965	5,965	23,088	915,398	919,264	47	8,000,908	7,369,179,354	0.75	153.46	3.87	39.65	5.11
Events excluding code 788													
00 to 01 year	76	76	182	6,231	6,404	0	3,797,628	1,270,322,579	0.02	81.99	2.39	34.24	0.00
02 to 04 years	575	575	2,217	76,430	78,169	1	5,799,394	2,878,653,678	0.10	132.92	3.86	34.47	1.28
05 to 09 years	4,082	4,082	19,455	625,704	650,679	2	8,390,587	5,107,843,244	0.49	153.28	4.77	32.16	0.31
10 to 16 years	21,124	21,124	89,213	2,866,546	3,013,004	27	11,197,597	7,714,968,151	1.89	135.70	4.22	32.13	0.90
17 to 39 years	94,256	94,256	307,675	10,090,957	10,586,590	383	35,687,670	23,048,727,184	2.64	107.06	3.26	32.80	3.62
40 to 64 years	63,386	63,386	247,428	8,883,350	9,072,303	360	33,175,922	27,548,951,119	1.91	140.15	3.90	35.90	3.97
65+ years	5,974	5,974	23,117	917,103	920,535	47	8,001,621	7,373,052,176	0.75	153.52	3.87	39.67	5.11

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Lamotrigine (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
00 to 01 year	218	218	1,094	36,468	37,276	0	3,800,716	1,272,502,426	0.06	167.28	5.02	33.33	0.00
02 to 04 years	1,148	1,148	5,941	205,604	211,124	2	5,805,613	2,884,941,999	0.20	179.10	5.18	34.61	0.95
05 to 09 years	5,769	5,769	31,096	1,011,317	1,052,849	7	8,405,018	5,127,247,325	0.69	175.30	5.39	32.52	0.66
10 to 16 years	26,332	26,332	127,170	4,148,910	4,349,522	39	11,227,109	7,765,485,744	2.35	157.56	4.83	32.62	0.90
17 to 39 years	144,986	144,986	558,350	18,539,105	19,477,914	851	36,031,039	23,682,023,333	4.02	127.87	3.85	33.20	4.37
40 to 64 years	119,012	119,012	558,790	20,417,892	20,918,590	975	34,142,649	29,393,882,057	3.49	171.56	4.70	36.54	4.66
65+ years	12,496	12,496	54,799	2,207,840	2,224,900	144	8,396,421	8,121,301,240	1.49	176.68	4.39	40.29	6.47
Events excluding code 788													
00 to 01 year	218	218	1,094	36,468	37,276	0	3,800,799	1,272,596,481	0.06	167.28	5.02	33.33	0.00
02 to 04 years	1,148	1,148	5,941	205,604	211,124	2	5,805,667	2,885,200,724	0.20	179.10	5.18	34.61	0.95
05 to 09 years	5,770	5,770	31,100	1,011,437	1,053,236	5	8,405,107	5,127,612,973	0.69	175.29	5.39	32.52	0.47
10 to 16 years	26,342	26,342	127,237	4,150,848	4,352,433	33	11,227,263	7,766,166,473	2.35	157.58	4.83	32.62	0.76
17 to 39 years	145,161	145,161	558,945	18,557,029	19,510,957	759	36,033,511	23,692,160,774	4.03	127.84	3.85	33.20	3.89
40 to 64 years	119,123	119,123	559,113	20,428,848	20,950,811	891	34,144,759	29,409,067,635	3.49	171.49	4.69	36.54	4.25
65+ years	12,511	12,511	54,882	2,211,007	2,229,943	139	8,397,111	8,125,874,466	1.49	176.73	4.39	40.29	6.23

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Levetiracetam													
Incident to All AEDs													
Events including code 788													
00 to 01 year	1,814	1,814	8,784	287,019	288,120	1	3,797,546	1,270,205,700	0.48	158.22	4.84	32.68	0.35
02 to 04 years	3,009	3,009	16,135	532,979	534,401	2	5,798,778	2,878,013,477	0.52	177.13	5.36	33.03	0.37
05 to 09 years	3,780	3,780	19,090	637,113	643,710	7	8,389,795	5,107,276,768	0.45	168.55	5.05	33.37	1.09
10 to 16 years	5,702	5,702	26,043	870,969	886,017	8	11,198,026	7,716,711,347	0.51	152.75	4.57	33.44	0.90
17 to 39 years	19,274	19,274	61,431	2,018,257	2,068,312	66	35,690,914	23,057,071,665	0.54	104.71	3.19	32.85	3.19
40 to 64 years	29,209	29,209	97,786	3,324,738	3,366,047	191	33,177,284	27,545,046,365	0.88	113.83	3.35	34.00	5.67
65+ years	20,631	20,631	78,309	2,894,233	2,905,540	155	8,001,148	7,367,639,641	2.58	140.29	3.80	36.96	5.33
Events excluding code 788													
00 to 01 year	1,815	1,815	8,785	287,049	288,129	1	3,797,628	1,270,299,157	0.48	158.15	4.84	32.67	0.35
02 to 04 years	3,009	3,009	16,135	532,979	534,541	1	5,798,832	2,878,270,856	0.52	177.13	5.36	33.03	0.19
05 to 09 years	3,781	3,781	19,110	637,773	644,339	7	8,389,884	5,107,638,130	0.45	168.68	5.05	33.37	1.09
10 to 16 years	5,705	5,705	26,046	871,039	886,089	8	11,198,181	7,717,376,259	0.51	152.68	4.57	33.44	0.90
17 to 39 years	19,288	19,288	61,486	2,019,877	2,070,466	58	35,693,420	23,066,446,774	0.54	104.72	3.19	32.85	2.80
40 to 64 years	29,243	29,243	97,905	3,328,229	3,371,434	178	33,179,427	27,558,361,443	0.88	113.81	3.35	33.99	5.28
65+ years	20,651	20,651	78,400	2,897,837	2,910,133	147	8,001,862	7,371,513,080	2.58	140.32	3.80	36.96	5.05

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Levetiracetam (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
00 to 01 year	2,449	2,449	14,467	471,456	477,179	3	3,799,668	1,271,711,416	0.64	192.51	5.91	32.59	0.63
02 to 04 years	4,054	4,054	26,184	868,134	881,527	4	5,802,799	2,882,488,015	0.70	214.14	6.46	33.16	0.45
05 to 09 years	5,592	5,592	35,167	1,177,332	1,203,123	10	8,403,012	5,126,074,996	0.67	210.54	6.29	33.48	0.83
10 to 16 years	8,616	8,616	50,458	1,710,300	1,752,036	18	11,234,016	7,777,813,646	0.77	198.50	5.86	33.90	1.03
17 to 39 years	34,324	34,324	146,235	4,956,377	5,130,725	177	36,100,669	23,790,180,841	0.95	144.40	4.26	33.89	3.45
40 to 64 years	57,494	57,494	250,665	8,876,922	9,089,671	495	34,215,043	29,498,355,663	1.68	154.40	4.36	35.41	5.45
65+ years	32,844	32,844	145,570	5,532,916	5,603,614	316	8,396,626	8,112,951,098	3.91	168.46	4.43	38.01	5.64
Events excluding code 788													
00 to 01 year	2,450	2,450	14,468	471,486	477,188	3	3,799,751	1,271,805,470	0.64	192.44	5.91	32.59	0.63
02 to 04 years	4,054	4,054	26,184	868,134	881,686	2	5,802,853	2,882,746,007	0.70	214.14	6.46	33.16	0.23
05 to 09 years	5,593	5,593	35,190	1,178,262	1,205,172	8	8,403,102	5,126,440,985	0.67	210.67	6.29	33.48	0.66
10 to 16 years	8,620	8,620	50,465	1,710,467	1,752,217	18	11,234,169	7,778,500,293	0.77	198.43	5.85	33.89	1.03
17 to 39 years	34,364	34,364	146,348	4,959,705	5,136,754	159	36,103,146	23,800,458,483	0.95	144.33	4.26	33.89	3.10
40 to 64 years	57,566	57,566	250,884	8,884,001	9,102,390	464	34,217,171	29,513,635,703	1.68	154.33	4.36	35.41	5.10
65+ years	32,873	32,873	145,719	5,538,634	5,613,267	295	8,397,317	8,117,519,587	3.91	168.49	4.43	38.01	5.26

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Topiramate													
Incident to All AEDs													
Events including code 788													
00 to 01 year	271	271	1,048	33,162	33,054	0	3,797,546	1,270,226,290	0.07	122.37	3.87	31.64	0.00
02 to 04 years	405	405	1,256	41,406	43,277	1	5,799,265	2,878,368,741	0.07	102.24	3.10	32.97	2.31
05 to 09 years	3,656	3,656	10,633	340,717	367,918	5	8,390,490	5,107,435,333	0.44	93.19	2.91	32.04	1.36
10 to 16 years	24,281	24,281	57,523	1,864,998	2,063,288	42	11,197,165	7,712,442,416	2.17	76.81	2.37	32.42	2.04
17 to 39 years	158,811	158,811	374,908	12,306,040	13,370,879	1,006	35,683,340	23,018,092,531	4.45	77.49	2.36	32.82	7.52
40 to 64 years	149,680	149,680	401,711	14,185,032	15,034,113	1,124	33,165,167	27,499,651,129	4.51	94.77	2.68	35.31	7.48
65+ years	10,763	10,763	26,019	1,020,795	1,062,638	83	7,999,377	7,366,462,719	1.35	94.84	2.42	39.23	7.81
Events excluding code 788													
00 to 01 year	271	271	1,048	33,162	33,054	0	3,797,628	1,270,319,747	0.07	122.37	3.87	31.64	0.00
02 to 04 years	405	405	1,256	41,406	43,277	1	5,799,319	2,878,626,303	0.07	102.24	3.10	32.97	2.31
05 to 09 years	3,658	3,658	10,638	340,867	368,996	3	8,390,579	5,107,796,742	0.44	93.18	2.91	32.04	0.81
10 to 16 years	24,288	24,288	57,532	1,865,229	2,063,751	38	11,197,320	7,713,104,855	2.17	76.80	2.37	32.42	1.84
17 to 39 years	158,978	158,978	375,296	12,318,149	13,394,603	929	35,685,841	23,027,390,146	4.45	77.48	2.36	32.82	6.94
40 to 64 years	149,822	149,822	402,032	14,195,699	15,056,003	1,034	33,167,281	27,512,872,851	4.52	94.75	2.68	35.31	6.87
65+ years	10,776	10,776	26,041	1,021,447	1,064,048	78	8,000,087	7,370,329,830	1.35	94.79	2.42	39.22	7.33

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Topiramate (continued)													
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788													
00 to 01 year	804	804	5,239	166,441	169,439	7	3,800,778	1,272,542,385	0.21	207.02	6.52	31.77	4.13
02 to 04 years	1,109	1,109	6,251	207,844	213,318	8	5,805,957	2,885,387,348	0.19	187.42	5.64	33.25	3.75
05 to 09 years	5,092	5,092	20,191	660,077	701,318	16	8,408,145	5,130,876,206	0.61	129.63	3.97	32.69	2.28
10 to 16 years	29,037	29,037	81,420	2,684,467	2,944,269	61	11,238,903	7,779,650,218	2.58	92.45	2.80	32.97	2.07
17 to 39 years	211,682	211,682	562,499	18,599,535	20,190,695	1,648	36,111,606	23,759,473,339	5.86	87.87	2.66	33.07	8.16
40 to 64 years	230,203	230,203	700,274	24,962,217	26,488,308	2,034	34,223,038	29,458,370,633	6.73	108.44	3.04	35.65	7.68
65+ years	19,859	19,859	55,102	2,163,403	2,271,224	171	8,403,949	8,129,146,934	2.36	108.94	2.77	39.26	7.53
Events excluding code 788													
00 to 01 year	804	804	5,239	166,441	169,439	7	3,800,861	1,272,636,440	0.21	207.02	6.52	31.77	4.13
02 to 04 years	1,109	1,109	6,251	207,844	213,371	8	5,806,011	2,885,646,073	0.19	187.42	5.64	33.25	3.75
05 to 09 years	5,094	5,094	20,196	660,227	702,396	14	8,408,235	5,131,243,302	0.61	129.61	3.96	32.69	1.99
10 to 16 years	29,048	29,048	81,442	2,685,088	2,946,207	54	11,239,056	7,780,334,845	2.58	92.44	2.80	32.97	1.83
17 to 39 years	211,926	211,926	563,131	18,619,867	20,232,648	1,517	36,114,075	23,769,635,566	5.87	87.86	2.66	33.06	7.50
40 to 64 years	230,453	230,453	700,955	24,985,254	26,537,856	1,859	34,225,133	29,473,511,374	6.73	108.42	3.04	35.64	7.01
65+ years	19,878	19,878	55,146	2,164,778	2,275,252	162	8,404,635	8,133,723,651	2.37	108.90	2.77	39.26	7.12

Table 3: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Lamotrigine													
Incident to All AEDs													
Events including code 788													
Female	121,791	121,791	425,526	14,495,530	15,035,230	530	46,243,058	38,120,222,232	2.63	119.02	3.49	34.06	3.53
Male	67,207	67,207	262,152	8,918,618	9,228,062	367	44,826,646	36,758,822,114	1.50	132.70	3.90	34.02	3.98
Unknown	320	320	1,192	38,438	40,581	0	108,682	109,391,570	2.94	120.12	3.73	32.25	0.00
Events excluding code 788													
Female	121,899	121,899	425,832	14,505,154	15,051,999	470	46,245,892	38,135,527,525	2.64	118.99	3.49	34.06	3.12
Male	67,254	67,254	262,263	8,922,729	9,235,104	350	44,828,642	36,771,390,645	1.50	132.67	3.90	34.02	3.79
Unknown	320	320	1,192	38,438	40,581	0	108,684	109,421,815	2.94	120.12	3.73	32.25	0.00
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
Female	203,260	203,260	850,341	29,616,686	30,779,615	1,249	47,206,507	40,213,247,501	4.31	145.71	4.18	34.83	4.06
Male	106,279	106,279	485,098	16,891,060	17,429,902	767	45,421,490	37,996,474,066	2.34	158.93	4.56	34.82	4.40
Unknown	422	422	1,801	59,390	62,658	2	109,221	111,607,770	3.86	140.73	4.27	32.98	3.19
Events excluding code 788													
Female	203,477	203,477	851,055	29,639,038	30,828,408	1,111	47,209,286	40,230,778,560	4.31	145.66	4.18	34.83	3.60
Male	106,373	106,373	485,452	16,902,693	17,454,487	717	45,423,434	38,010,212,203	2.34	158.90	4.56	34.82	4.11
Unknown	423	423	1,805	59,510	62,885	1	109,221	111,639,964	3.87	140.69	4.27	32.97	1.59

Table 3: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Levetiracetam													
Incident to All AEDs													
Events including code 788													
Female	43,133	43,133	156,754	5,380,332	5,437,063	194	46,243,072	38,139,524,045	0.93	124.74	3.63	34.32	3.57
Male	40,210	40,210	150,499	5,175,133	5,245,020	235	44,826,651	36,766,764,361	0.90	128.70	3.74	34.39	4.48
Unknown	76	76	325	9,843	10,064	1	108,682	109,490,246	0.70	129.51	4.28	30.29	9.94
Events excluding code 788													
Female	43,184	43,184	156,990	5,388,213	5,446,686	179	46,245,906	38,154,867,023	0.93	124.77	3.64	34.32	3.29
Male	40,232	40,232	150,552	5,176,727	5,248,381	220	44,828,647	36,779,337,862	0.90	128.67	3.74	34.38	4.19
Unknown	76	76	325	9,843	10,064	1	108,684	109,520,491	0.70	129.51	4.28	30.29	9.94
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
Female	77,535	77,535	347,946	12,257,575	12,555,194	460	47,287,566	40,366,264,129	1.64	158.09	4.49	35.23	3.66
Male	67,709	67,709	320,160	11,316,220	11,562,254	561	45,456,180	38,055,259,212	1.49	167.13	4.73	35.35	4.85
Unknown	129	129	640	19,642	20,427	2	109,283	111,955,325	1.18	152.26	4.96	30.69	9.79
Events excluding code 788													
Female	77,635	77,635	348,321	12,270,006	12,575,783	417	47,290,354	40,383,989,989	1.64	158.05	4.49	35.23	3.32
Male	67,756	67,756	320,297	11,321,041	11,572,426	531	45,458,121	38,069,037,406	1.49	167.09	4.73	35.35	4.59
Unknown	129	129	640	19,642	20,465	1	109,283	111,988,112	1.18	152.26	4.96	30.69	4.89

Table 3: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Topiramate													
Incident to All AEDs													
Events including code 788													
Female	281,831	281,831	721,661	24,673,596	26,453,175	1,698	46,243,038	38,065,217,442	6.09	87.55	2.56	34.19	6.42
Male	65,482	65,482	149,909	5,070,873	5,470,091	560	44,826,649	36,751,981,669	1.46	77.44	2.29	33.83	10.24
Unknown	554	554	1,528	47,681	51,901	3	108,682	109,295,140	5.10	86.07	2.76	31.20	5.78
Events excluding code 788													
Female	282,103	282,103	722,318	24,694,846	26,495,407	1,554	46,245,872	38,080,414,420	6.10	87.54	2.56	34.19	5.87
Male	65,541	65,541	149,997	5,073,432	5,476,424	526	44,828,645	36,764,521,876	1.46	77.41	2.29	33.82	9.60
Unknown	554	554	1,528	47,681	51,901	3	108,684	109,325,258	5.10	86.07	2.76	31.20	5.78
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788													
Female	399,206	399,206	1,163,238	40,267,513	43,134,847	2,975	47,317,640	40,299,473,473	8.44	100.87	2.91	34.62	6.90
Male	97,872	97,872	265,648	9,110,218	9,771,283	966	45,482,405	38,078,148,296	2.15	93.08	2.71	34.29	9.89
Unknown	708	708	2,090	66,253	72,441	4	109,305	111,774,638	6.48	93.58	2.95	31.70	5.52
Events excluding code 788													
Female	399,644	399,644	1,164,453	40,307,759	43,220,132	2,705	47,320,426	40,316,981,948	8.45	100.86	2.91	34.62	6.26
Male	97,960	97,960	265,817	9,115,487	9,784,596	912	45,484,348	38,091,897,154	2.15	93.05	2.71	34.29	9.32
Unknown	708	708	2,090	66,253	72,441	4	109,305	111,807,481	6.48	93.58	2.95	31.70	5.52

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Lamotrigine													
Incident to All AEDs													
Events including code 788													
2004	7,191	7,191	30,405	1,081,337	1,119,398	36	18,956,673	4,111,101,254	0.38	150.37	4.23	35.56	3.22
2005	12,062	12,062	50,940	1,774,107	1,835,115	60	20,901,943	5,877,196,816	0.58	147.08	4.22	34.83	3.27
2006	15,317	15,317	65,561	2,328,438	2,410,518	83	22,346,613	6,164,572,353	0.69	152.02	4.28	35.52	3.44
2007	18,416	18,416	76,762	2,704,492	2,794,638	94	24,900,789	6,562,434,178	0.74	146.86	4.17	35.23	3.36
2008	29,349	29,349	115,160	3,871,863	4,043,732	138	45,482,041	10,104,578,729	0.65	131.92	3.92	33.62	3.41
2009	35,205	35,205	130,853	4,376,511	4,571,936	176	46,501,410	12,990,807,045	0.76	124.32	3.72	33.45	3.85
2010	31,935	31,935	113,368	3,807,341	3,963,017	147	44,686,345	12,535,870,606	0.71	119.22	3.55	33.58	3.71
2011	28,311	28,311	82,284	2,731,039	2,833,391	120	43,137,458	12,058,615,000	0.66	96.47	2.91	33.19	4.24
2012	11,532	11,532	23,537	777,458	732,128	43	24,798,929	4,583,259,935	0.47	67.42	2.04	33.03	5.87
Events excluding code 788													
2004	7,194	7,194	30,428	1,082,937	1,120,642	36	18,958,374	4,112,748,812	0.38	150.53	4.23	35.59	3.21
2005	12,070	12,070	50,953	1,774,462	1,836,931	54	20,903,510	5,879,482,139	0.58	147.01	4.22	34.83	2.94
2006	15,333	15,333	65,596	2,329,559	2,412,804	72	22,348,184	6,166,874,567	0.69	151.93	4.28	35.51	2.98
2007	18,427	18,427	76,791	2,705,467	2,797,321	86	24,903,378	6,564,816,602	0.74	146.82	4.17	35.23	3.07
2008	29,376	29,376	115,264	3,874,957	4,048,705	127	45,486,297	10,108,533,073	0.65	131.91	3.92	33.62	3.14
2009	35,242	35,242	130,940	4,379,262	4,576,686	159	46,504,574	12,995,836,538	0.76	124.26	3.72	33.44	3.47
2010	31,966	31,966	113,439	3,809,522	3,966,627	134	44,689,274	12,540,448,783	0.72	119.17	3.55	33.58	3.38
2011	28,328	28,328	82,328	2,732,369	2,835,283	115	43,139,995	12,062,754,209	0.66	96.45	2.91	33.19	4.06
2012	11,537	11,537	23,548	777,786	732,685	37	24,801,003	4,584,845,262	0.47	67.42	2.04	33.03	5.05

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Lamotrigine (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
2004	14,287	14,287	80,177	2,898,361	2,982,171	121	19,462,181	4,302,537,298	0.73	202.87	5.61	36.15	4.06
2005	21,671	21,671	113,392	4,087,419	4,225,731	145	21,415,401	6,139,289,470	1.01	188.61	5.23	36.05	3.43
2006	25,094	25,094	131,909	4,835,100	4,994,439	187	22,818,854	6,412,353,306	1.10	192.68	5.26	36.65	3.74
2007	29,725	29,725	150,737	5,441,623	5,620,929	217	25,528,448	6,839,012,183	1.16	183.07	5.07	36.10	3.86
2008	47,243	47,243	221,161	7,598,802	7,926,872	307	46,612,429	10,549,399,765	1.01	160.85	4.68	34.36	3.87
2009	56,273	56,273	243,718	8,318,081	8,692,687	382	47,602,748	13,561,775,156	1.18	147.82	4.33	34.13	4.39
2010	51,455	51,455	208,572	7,115,151	7,426,095	309	45,793,217	13,095,877,800	1.12	138.28	4.05	34.11	4.16
2011	45,243	45,243	146,401	4,912,145	5,113,093	269	44,221,996	12,603,870,978	1.02	108.57	3.24	33.55	5.26
2012	18,970	18,970	41,173	1,360,454	1,290,158	81	25,629,969	4,817,213,381	0.74	71.72	2.17	33.04	6.28
Events excluding code 788													
2004	14,305	14,305	80,284	2,902,534	2,988,830	109	19,463,834	4,304,421,387	0.73	202.90	5.61	36.15	3.65
2005	21,687	21,687	113,469	4,089,685	4,231,604	129	21,416,915	6,141,863,653	1.01	188.58	5.23	36.04	3.05
2006	25,125	25,125	131,999	4,838,029	5,002,406	165	22,820,352	6,414,894,303	1.10	192.56	5.25	36.65	3.30
2007	29,756	29,756	150,828	5,444,420	5,629,193	193	25,531,137	6,841,649,970	1.17	182.97	5.07	36.10	3.43
2008	47,295	47,295	221,367	7,605,000	7,940,326	278	46,616,590	10,553,824,733	1.01	160.80	4.68	34.35	3.50
2009	56,342	56,342	243,962	8,325,979	8,709,371	347	47,605,807	13,567,415,602	1.18	147.78	4.33	34.13	3.98
2010	51,506	51,506	208,720	7,119,706	7,435,905	280	45,796,010	13,101,007,198	1.12	138.23	4.05	34.11	3.77
2011	45,275	45,275	146,489	4,914,757	5,116,774	256	44,224,452	12,608,530,535	1.02	108.55	3.24	33.55	5.00
2012	18,982	18,982	41,194	1,361,131	1,291,371	72	25,631,996	4,819,023,346	0.74	71.71	2.17	33.04	5.58

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Levetiracetam													
Incident to All AEDs													
Events including code 788													
2004	2,025	2,025	8,060	275,399	285,267	12	18,956,673	4,111,112,560	0.11	136.00	3.98	34.17	4.21
2005	2,966	2,966	11,857	411,223	422,679	19	20,903,714	5,877,538,224	0.14	138.65	4.00	34.68	4.50
2006	3,877	3,877	17,752	622,210	636,657	20	22,351,812	6,165,689,911	0.17	160.49	4.58	35.05	3.14
2007	5,838	5,838	24,251	849,780	860,425	41	24,910,160	6,564,577,485	0.23	145.56	4.15	35.04	4.77
2008	10,816	10,816	46,582	1,606,370	1,644,280	57	45,495,796	10,107,789,513	0.24	148.52	4.31	34.48	3.47
2009	16,366	16,366	67,894	2,307,237	2,355,637	77	46,521,648	12,995,503,761	0.35	140.98	4.15	33.98	3.27
2010	16,925	16,925	65,292	2,228,320	2,261,965	107	44,712,814	12,542,295,088	0.38	131.66	3.86	34.13	4.73
2011	16,774	16,774	50,201	1,739,402	1,751,275	71	43,168,516	12,066,192,549	0.39	103.70	2.99	34.65	4.05
2012	7,832	7,832	15,689	525,367	473,962	26	24,810,451	4,585,079,561	0.32	67.08	2.00	33.49	5.49
Events excluding code 788													
2004	2,028	2,028	8,064	275,514	285,553	10	18,958,374	4,112,760,118	0.11	135.86	3.98	34.17	3.50
2005	2,970	2,970	11,861	411,318	422,910	16	20,905,281	5,879,823,748	0.14	138.49	3.99	34.68	3.78
2006	3,878	3,878	17,753	622,240	637,246	18	22,353,387	6,167,993,818	0.17	160.45	4.58	35.05	2.82
2007	5,841	5,841	24,278	850,592	860,657	40	24,912,753	6,566,963,327	0.23	145.62	4.16	35.04	4.65
2008	10,825	10,825	46,638	1,608,510	1,646,687	52	45,500,058	10,111,748,697	0.24	148.59	4.31	34.49	3.16
2009	16,384	16,384	67,985	2,310,253	2,360,092	72	46,524,825	13,000,540,456	0.35	141.01	4.15	33.98	3.05
2010	16,941	16,941	65,343	2,229,859	2,264,502	100	44,715,775	12,546,881,851	0.38	131.62	3.86	34.13	4.42
2011	16,787	16,787	50,245	1,740,815	1,753,167	68	43,171,095	12,070,345,060	0.39	103.70	2.99	34.65	3.88
2012	7,838	7,838	15,700	525,682	474,317	24	24,812,537	4,586,668,301	0.32	67.07	2.00	33.48	5.06

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Levetiracetam (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
2004	5,934	5,934	33,354	1,198,198	1,236,486	45	19,475,277	4,306,443,292	0.30	201.92	5.62	35.92	3.64
2005	7,683	7,683	41,234	1,471,105	1,511,065	49	21,437,980	6,147,995,804	0.36	191.48	5.37	35.68	3.24
2006	8,450	8,450	52,259	1,894,738	1,943,358	52	22,853,963	6,424,973,539	0.37	224.23	6.18	36.26	2.68
2007	11,333	11,333	63,730	2,305,290	2,354,088	85	25,581,339	6,856,637,919	0.44	203.41	5.62	36.17	3.61
2008	19,274	19,274	103,601	3,670,392	3,777,056	140	46,720,912	10,579,522,858	0.41	190.43	5.38	35.43	3.71
2009	27,568	27,568	139,318	4,872,314	5,004,278	223	47,725,828	13,602,843,119	0.58	176.74	5.05	34.97	4.46
2010	27,278	27,278	121,779	4,244,377	4,367,023	216	45,921,382	13,137,788,213	0.59	155.60	4.46	34.85	4.95
2011	25,953	25,953	87,978	3,074,845	3,147,381	159	44,352,939	12,645,488,674	0.59	118.48	3.39	34.95	5.05
2012	11,900	11,900	25,493	862,178	797,140	54	25,701,825	4,831,785,248	0.46	72.45	2.14	33.82	6.77
Events excluding code 788													
2004	5,945	5,945	33,392	1,199,395	1,238,088	39	19,476,938	4,308,331,895	0.31	201.75	5.62	35.92	3.15
2005	7,691	7,691	41,248	1,471,500	1,513,252	42	21,439,494	6,150,576,742	0.36	191.33	5.36	35.67	2.78
2006	8,456	8,456	52,267	1,894,968	1,945,135	49	22,855,457	6,427,528,088	0.37	224.10	6.18	36.26	2.52
2007	11,339	11,339	63,760	2,306,172	2,355,053	84	25,584,047	6,859,297,210	0.44	203.38	5.62	36.17	3.57
2008	19,291	19,291	103,690	3,673,812	3,782,107	129	46,725,090	10,583,980,841	0.41	190.44	5.38	35.43	3.41
2009	27,602	27,602	139,454	4,876,641	5,013,845	201	47,728,923	13,608,527,542	0.58	176.68	5.05	34.97	4.01
2010	27,306	27,306	121,880	4,248,100	4,372,533	201	45,924,223	13,142,968,096	0.59	155.57	4.46	34.85	4.60
2011	25,979	25,979	88,052	3,077,301	3,150,826	152	44,355,466	12,650,193,487	0.59	118.45	3.39	34.95	4.82
2012	11,911	11,911	25,515	862,800	797,835	52	25,703,889	4,833,611,606	0.46	72.44	2.14	33.82	6.52

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Topiramate													
Incident to All AEDs													
Events including code 788													
2004	17,999	17,999	53,659	1,830,939	1,952,561	115	18,956,672	4,111,040,356	0.95	101.72	2.98	34.12	5.89
2005	27,094	27,094	78,042	2,664,172	2,863,664	184	20,895,296	5,875,773,110	1.30	98.33	2.88	34.14	6.43
2006	26,852	26,852	78,866	2,773,753	2,953,359	213	22,331,148	6,160,788,570	1.20	103.30	2.94	35.17	7.21
2007	29,159	29,159	82,343	2,919,498	3,109,301	231	24,879,131	6,556,799,988	1.17	100.12	2.82	35.46	7.43
2008	46,216	46,216	120,022	4,123,380	4,456,413	314	45,455,721	10,097,629,131	1.02	89.22	2.60	34.36	7.05
2009	63,984	63,984	164,889	5,530,539	5,976,037	425	46,466,826	12,981,539,816	1.38	86.44	2.58	33.54	7.11
2010	61,119	61,119	149,906	5,047,678	5,469,264	400	44,637,854	12,522,943,072	1.37	82.59	2.45	33.67	7.31
2011	51,216	51,216	106,307	3,592,509	3,912,081	294	43,077,751	12,042,898,983	1.19	70.14	2.08	33.79	7.52
2012	24,228	24,228	39,064	1,309,682	1,282,487	85	24,761,649	4,577,081,225	0.98	54.06	1.61	33.53	6.63
Events excluding code 788													
2004	18,024	18,024	53,715	1,832,648	1,956,088	103	18,958,373	4,112,687,756	0.95	101.68	2.98	34.12	5.27
2005	27,119	27,119	78,089	2,665,335	2,866,957	168	20,896,840	5,878,054,566	1.30	98.28	2.88	34.13	5.86
2006	26,881	26,881	79,001	2,778,178	2,960,363	200	22,332,695	6,163,081,197	1.20	103.35	2.94	35.17	6.76
2007	29,182	29,182	82,397	2,921,279	3,113,069	215	24,881,682	6,559,168,571	1.17	100.11	2.82	35.45	6.91
2008	46,264	46,264	120,120	4,126,487	4,464,177	291	45,459,936	10,101,567,985	1.02	89.19	2.60	34.35	6.52
2009	64,051	64,051	165,024	5,534,508	5,984,774	389	46,469,935	12,986,548,083	1.38	86.41	2.58	33.54	6.50
2010	61,166	61,166	150,003	5,051,074	5,477,141	374	44,640,725	12,527,491,748	1.37	82.58	2.45	33.67	6.83
2011	51,256	51,256	106,381	3,595,305	3,916,941	267	43,080,228	12,047,005,944	1.19	70.14	2.08	33.80	6.82
2012	24,255	24,255	39,113	1,311,145	1,284,222	76	24,763,680	4,578,655,704	0.98	54.06	1.61	33.52	5.92

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Topiramate (continued)													
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788													
2004	30,325	30,325	111,020	3,778,898	4,019,140	253	19,483,927	4,309,318,944	1.56	124.61	3.66	34.04	6.29
2005	40,888	40,888	136,820	4,792,897	5,121,177	331	21,433,876	6,149,312,246	1.91	117.22	3.35	35.03	6.46
2006	38,182	38,182	131,998	4,724,454	5,017,858	342	22,833,747	6,421,467,040	1.67	123.74	3.46	35.79	6.82
2007	41,285	41,285	134,290	4,822,153	5,136,369	368	25,552,072	6,850,313,477	1.62	116.80	3.25	35.91	7.16
2008	65,511	65,511	195,290	6,810,893	7,337,178	542	46,699,121	10,574,703,622	1.40	103.97	2.98	34.88	7.39
2009	89,983	89,983	263,862	8,962,602	9,661,537	756	47,688,683	13,598,235,896	1.89	99.60	2.93	33.97	7.82
2010	86,104	86,104	236,615	8,053,418	8,717,408	707	45,862,825	13,127,090,080	1.88	93.53	2.75	34.04	8.11
2011	71,710	71,710	163,702	5,571,880	6,067,544	517	44,276,381	12,630,514,238	1.62	77.70	2.28	34.04	8.52
2012	33,798	33,798	57,379	1,926,789	1,900,360	129	25,670,058	4,828,440,864	1.32	57.01	1.70	33.58	6.79
Events excluding code 788													
2004	30,372	30,372	111,149	3,782,720	4,029,096	226	19,485,585	4,311,211,483	1.56	124.55	3.66	34.03	5.61
2005	40,926	40,926	136,887	4,794,667	5,127,578	302	21,435,355	6,151,890,836	1.91	117.15	3.34	35.03	5.89
2006	38,229	38,229	132,212	4,732,572	5,033,331	320	22,835,191	6,424,003,037	1.67	123.80	3.46	35.80	6.36
2007	41,323	41,323	134,374	4,824,905	5,142,804	339	25,554,713	6,852,944,718	1.62	116.76	3.25	35.91	6.59
2008	65,589	65,589	195,511	6,817,748	7,351,896	501	46,703,221	10,579,133,209	1.40	103.95	2.98	34.87	6.81
2009	90,086	90,086	264,079	8,969,780	9,677,554	693	47,691,642	13,603,881,892	1.89	99.57	2.93	33.97	7.16
2010	86,181	86,181	236,865	8,061,474	8,733,736	662	45,865,510	13,132,214,483	1.88	93.54	2.75	34.03	7.58
2011	71,773	71,773	163,836	5,576,736	6,078,232	463	44,278,746	12,635,158,803	1.62	77.70	2.28	34.04	7.62
2012	33,833	33,833	57,447	1,928,897	1,902,942	115	25,672,039	4,830,248,122	1.32	57.01	1.70	33.58	6.04

Appendix A. Diagnosis and procedure codes used to define kidney stone events

ICD-9 diagnosis codes

592.0	Calculus of kidney (excludes uric acid stone)
592.1	Calculus of ureter
592.9	Urinary calculus, unspecified
274.11	Uric acid nephrolithiasis
788.0	Renal colic
594	Calculus of lower urinary tract

ICD-9 procedure codes

55.04	Percutaneous fragmentation with fragmentation
55.92	Repeat nephroscopic removal during current episode
56.2	Ureterotomy for removal of calculus or exploration
59.8	Transurethral ureteral stent placement for passage of calculus
59.95	Ultrasonic fragmentation of urinary stones
98.51	ESWL
55.04	percutaneous nephrostomy with fragmentation
98.51	Extracorporeal shockwave lithotripsy of the kidney, ureter, or bladder
59.95	ultrasonic fragmentation of urinary stones

CPT codes

50060	Nephrolithotomy; removal of calculus
50065	Secondary surgical operation for calculus
50070	Nephrolithotomy complicated by congenital kidney abnormality
50075	Removal of large staghorn calculus filling renal pelvis (includes anatomic pyelolithotomy)
50080	Percutaneous nephrostolithotomy with or without lithotripsy, up to 2 cm
50081	PCNL, over 2 cm
50130	Pyelotomy, with removal of calculus
50590	ESWL
50610	Ureterolithotomy; upper one third of ureter
50620	Ureterolithotomy, middle one third of ureter
50630	Ureterolithotomy, lower one third of ureter
52320	Cysto, ureteral cath, removal of calculus

Appendix A. Diagnosis and procedure codes used to define kidney stone events

CPT codes (continued)

52325	With fragmentation of calculus (ultrasound or EHL)
52330	With manipulation, but not removal of stone
52336	With removal of stone
52337	With lithotripsy
50945	Laproscopy, surgical; ureterolithotomy
50561	Renal endoscopy through established nephrostomy or pyelostomy; with removal for foreign body or calculus
50580	Renal endoscopy through nephrotomy or pyelotomy, with or without irrigation, instillation or ureteropyelography, exclusive of radiologic service; with removal of foreign body or calculus
51060	transvesical ureterolithotomy
51065	Cystotomy, with calculus basket extraction and/or ultrasonic or electrohydraulic fragmentation of urethral calculus
50080	Percutaneous nephrostolithotomy or pyelostolithotomy, with or without dilation, endoscopy, lithotripsy, stenting: up to 2cm
50081	Percutaneous nephrostolithotomy or pyelostolithotomy, with or without dilation, endoscopy, lithotripsy, stenting: over 2cm
50060	Nephrolithotomy; removal of calculus
50070	Nephrolithotomy; complicated by congenital kidney abnormality
50075	Nephrolithotomy; removal of large staghorn calculus filling renal pelvis and calyces
50610	Ureterolithotomy; upper one-third of ureter
50620	Ureterolithotomy; middle one-third of ureter
50630	Ureterolithotomy; lower one-third of ureter
50590	Lithotripsy, extracorporeal shock wave
52320	Cystourethroscopy with removal of ureteral calculus
52325	cystourethroscopy with fragmentation of ureteral calculus
52352	Cystourethroscopy with ureteroscopy; with removal or manipulation of calculus
52353	Cystourethroscopy with ureteroscopy; with lithotripsy
