

Disclaimer

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 for Request to09y05_mpr_wp26_v01, Report 2 of 2

Request ID: to09y05_mpr_wp26_v01, Report 2 of 2

Request Description: This report investigated diagnosis of agranulocytosis following new use of several anti-epileptic drugs (AEDs), as well as clozapine and olanzapine.

Sentinel Modular Program Tool Used: Modular Program #3 (MP3)

Data Source: Data from January 1, 2000 to May 31, 2013 from 18 Data Partners contributing to the Mini-Sentinel Distributed Database (MSDD) were included in this request. The request was distributed to Data Partners on April 11, 2014. Please see Appendix A for dates of available data.

Study Design: The purpose of this request was to examine users, episodes, dispensings, and events of several anti-epileptic drugs, as well as clozapine and olanzapine, with varying incident definitions, agranulocytosis event washout periods (7 and 183 days), and agranulocytosis event primary diagnosis indicators (primary and nonsecondary). Please see Appendices B and C for generic names used to define exposure in this request. Please see Appendix D for International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes used to define outcomes. In total, 40 scenarios were examined in this request with differing exposures of interest, incidence criteria, event washout period, event care setting. This report gives results for scenarios 25-40, which required the exposures to be incident to all oral AEDs of interest. Please see Appendix D for more details on each scenario.

Cohort Eligibility Criteria: Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least six months (183 days) before their first valid dispensing of the exposure medication, during which gaps in coverage of up to 45 days were allowed. The following age groups were included in the cohort: <18, 18-<45, 45-<60, 65 + years.

Limitations: Algorithms used to define exposures and outcomes are imperfect; thus, it is possible that there may be misclassification.

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

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Glossary of Terms in Modular Program 3*

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

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).

Cohort Definition (drug/exposure)- Indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event occurs

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

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

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.

Event Deduplication - specifies how events are counted by the MP algorithm: A value of 0 counts all occurrences of an event group code of interest; a value of 1 de-duplicates occurrences of the same event code on the same day (i.e., de-duplicates at the exact match code level); and a value of 2 de-duplicates occurrences of the same event group code on the same day (e.g., de-duplicates at the GROUP level).

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment 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-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 365.23.

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 Episodes with Events - number of unique episodes during which at least one incident event occurs. Each episode may only be counted once.

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.

Number of Events - total number of incident events. An individual or a treatment episode can have more than one incident event provided that the incident event meets the event incidence criteria.

Principal Diagnosis (PDX) - 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.

Treatment Episode Truncation Indicator - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query 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.

*all terms may not be used in this report

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

Table 1: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, and Primary Diagnosis Indicator

	New Users	New Episodes	Days Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Days Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk
Carbamazepine																
<i>7-day event washout</i>																
Nonsecondary diagnosis	82,262	82,262	214,323	7,818,025	24,190,243	23,531.1	22	27	92,091,291	234,577,494.5	0.89	95.04	2.61	36.48	9.35	11.47
Primary diagnosis	82,263	82,263	214,324	7,818,035	24,190,263	23,532.6	14	19	92,091,294	234,577,858.7	0.89	95.04	2.61	36.48	5.95	8.07
<i>183-day event washout</i>																
Nonsecondary diagnosis	82,239	82,239	214,268	7,816,532	24,178,691	23,527.0	19	21	92,089,451	234,556,166.4	0.89	95.05	2.61	36.48	8.08	8.93
Primary diagnosis	82,247	82,247	214,279	7,816,802	24,179,651	23,529.4	12	14	92,090,255	234,563,535.3	0.89	95.04	2.61	36.48	5.10	5.95
Lamotrigine																
<i>7-day event washout</i>																
Nonsecondary diagnosis	208,781	208,781	798,996	26,826,796	47,941,796	79,186.6	25	26	92,091,325	234,562,286.0	2.27	128.49	3.83	33.58	3.16	3.28
Primary diagnosis	208,784	208,784	799,000	26,826,916	47,941,931	79,191.1	14	14	92,091,328	234,562,648.9	2.27	128.49	3.83	33.58	1.77	1.77
<i>183-day event washout</i>																
Nonsecondary diagnosis	208,762	208,762	798,952	26,825,527	47,939,641	79,183.0	23	24	92,089,485	234,540,928.7	2.27	128.50	3.83	33.58	2.90	3.03
Primary diagnosis	208,770	208,770	798,968	26,825,982	47,940,216	79,188.2	14	14	92,090,289	234,548,302.0	2.27	128.50	3.83	33.58	1.77	1.77
Levetiracetam																
<i>7-day event washout</i>																
Nonsecondary diagnosis	104,254	104,254	410,921	13,531,243	42,721,086	39,532.9	266	308	92,091,325	234,649,368.4	1.13	129.79	3.94	32.93	67.29	77.91
Primary diagnosis	104,299	104,299	411,124	13,536,877	42,734,900	39,564.0	153	174	92,091,328	234,649,722.2	1.13	129.79	3.94	32.93	38.67	43.98
<i>183-day event washout</i>																
Nonsecondary diagnosis	103,890	103,890	409,801	13,499,495	42,619,860	39,444.1	231	261	92,089,485	234,628,165.4	1.13	129.94	3.94	32.94	58.56	66.17
Primary diagnosis	104,074	104,074	410,460	13,518,531	42,674,556	39,513.8	131	145	92,090,289	234,635,468.0	1.13	129.89	3.94	32.94	33.15	36.70
Topiramate																
<i>7-day event washout</i>																
Nonsecondary diagnosis	394,485	394,485	1,010,730	33,825,872	75,356,475	103,610.1	40	45	92,091,325	234,357,680.0	4.28	85.75	2.56	33.47	3.86	4.34
Primary diagnosis	394,495	394,495	1,010,742	33,826,187	75,357,214	103,613.1	29	34	92,091,328	234,358,038.6	4.28	85.75	2.56	33.47	2.80	3.28
<i>183-day event washout</i>																
Nonsecondary diagnosis	394,419	394,419	1,010,577	33,821,394	75,346,666	103,596.5	37	39	92,089,485	234,336,378.6	4.28	85.75	2.56	33.47	3.57	3.76
Primary diagnosis	394,460	394,460	1,010,636	33,823,065	75,350,217	103,603.8	27	31	92,090,289	234,343,716.0	4.28	85.75	2.56	33.47	2.61	2.99

Table 2: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Age Group

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member- Years	New Users/ 1K Eligible Members	Days Supplied / User	Dispensings/ User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk
Carbamazepine																
<i>7-day event washout</i>																
Nonsecondary diagnosis																
00 to 17 Years	9,976	9,976	42,520	1,557,217	6,997,715	4,542.8	3	6	23,076,158	57,196,346.2	0.43	156.10	4.26	36.62	6.60	13.21
18 to 44 Years	28,318	28,318	67,886	2,295,970	6,764,208	7,022.3	5	5	42,654,330	86,376,177.8	0.66	81.08	2.40	33.82	7.12	7.12
45 to 64 Years	27,521	27,521	66,830	2,460,433	6,671,578	7,438.7	7	8	26,257,320	66,467,714.7	1.05	89.40	2.43	36.82	9.41	10.75
65+ Years	16,447	16,447	37,087	1,504,405	3,756,741	4,527.4	7	8	8,272,266	24,537,255.8	1.99	91.47	2.25	40.56	15.46	17.67
Primary diagnosis																
00 to 17 Years	9,976	9,976	42,520	1,557,217	6,997,715	4,542.9	2	5	23,076,158	57,196,383.1	0.43	156.10	4.26	36.62	4.40	11.01
18 to 44 Years	28,318	28,318	67,886	2,295,970	6,764,208	7,023.4	1	1	42,654,330	86,376,246.4	0.66	81.08	2.40	33.82	1.42	1.42
45 to 64 Years	27,522	27,522	66,831	2,460,443	6,671,598	7,438.9	5	6	26,257,320	66,467,860.1	1.05	89.40	2.43	36.82	6.72	8.07
65+ Years	16,447	16,447	37,087	1,504,405	3,756,741	4,527.4	6	7	8,272,269	24,537,369.2	1.99	91.47	2.25	40.56	13.25	15.46
<i>183-day event washout</i>																
Nonsecondary diagnosis																
00 to 17 Years	9,973	9,973	42,495	1,556,469	6,988,372	4,541.0	2	2	23,075,892	57,192,929.7	0.43	156.07	4.26	36.63	4.40	4.40
18 to 44 Years	28,311	28,311	67,877	2,295,741	6,763,115	7,021.6	3	3	42,653,920	86,372,450.9	0.66	81.09	2.40	33.82	4.27	4.27
45 to 64 Years	27,514	27,514	66,821	2,460,222	6,671,100	7,438.0	7	8	26,256,441	66,459,985.9	1.05	89.42	2.43	36.82	9.41	10.76
65+ Years	16,441	16,441	37,075	1,504,100	3,756,104	4,526.4	7	8	8,271,675	24,530,799.9	1.99	91.48	2.26	40.57	15.46	17.67
Primary diagnosis																
00 to 17 Years	9,973	9,973	42,495	1,556,469	6,988,372	4,541.1	1	1	23,075,999	57,193,676.6	0.43	156.07	4.26	36.63	2.20	2.20
18 to 44 Years	28,315	28,315	67,883	2,295,911	6,763,875	7,023.3	0	0	42,654,120	86,374,018.7	0.66	81.08	2.40	33.82	0.00	0.00
45 to 64 Years	27,517	27,517	66,825	2,460,292	6,671,240	7,438.4	5	6	26,256,823	66,462,943.0	1.05	89.41	2.43	36.82	6.72	8.07
65+ Years	16,442	16,442	37,076	1,504,130	3,756,164	4,526.6	6	7	8,271,917	24,532,897.1	1.99	91.48	2.25	40.57	13.25	15.46

Table 2: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Age Group

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member- Years	New Users/ 1K Eligible Members	Days Supplied / User	Dispensings/ User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk
Lamotrigine																
7-day event washout																
Nonsecondary diagnosis																
00 to 17 Years	35,002	35,002	154,916	5,014,626	10,135,948	14,743.3	2	2	23,076,158	57,194,579.4	1.52	143.27	4.43	32.37	1.36	1.36
18 to 44 Years	117,552	117,552	413,229	13,429,948	23,143,590	40,001.4	14	15	42,648,060	86,331,636.5	2.76	114.25	3.52	32.50	3.50	3.75
45 to 64 Years	49,003	49,003	202,345	7,255,725	12,578,497	21,173.5	7	7	26,255,999	66,474,116.7	1.87	148.07	4.13	35.86	3.31	3.31
65+ Years	7,224	7,224	28,506	1,126,497	2,083,761	3,268.3	2	2	8,273,391	24,561,953.4	0.87	155.94	3.95	39.52	6.12	6.12
Primary diagnosis																
00 to 17 Years	35,004	35,004	154,919	5,014,716	10,136,053	14,744.2	0	0	23,076,158	57,194,615.0	1.52	143.26	4.43	32.37	0.00	0.00
18 to 44 Years	117,553	117,553	413,230	13,429,978	23,143,620	40,002.4	9	9	42,648,060	86,331,704.9	2.76	114.25	3.52	32.50	2.25	2.25
45 to 64 Years	49,003	49,003	202,345	7,255,725	12,578,497	21,176.2	3	3	26,255,999	66,474,262.1	1.87	148.07	4.13	35.86	1.42	1.42
65+ Years	7,224	7,224	28,506	1,126,497	2,083,761	3,268.3	2	2	8,273,394	24,562,066.9	0.87	155.94	3.95	39.52	6.12	6.12
183-day event washout																
Nonsecondary diagnosis																
00 to 17 Years	35,001	35,001	154,913	5,014,498	10,135,820	14,743.1	1	1	23,075,892	57,191,152.3	1.52	143.27	4.43	32.37	0.68	0.68
18 to 44 Years	117,545	117,545	413,212	13,429,424	23,142,472	39,999.8	14	15	42,647,650	86,327,910.4	2.76	114.25	3.52	32.50	3.50	3.75
45 to 64 Years	48,994	48,994	202,323	7,255,150	12,577,673	21,171.9	6	6	26,255,122	66,466,388.5	1.87	148.08	4.13	35.86	2.83	2.83
65+ Years	7,222	7,222	28,504	1,126,455	2,083,677	3,268.2	2	2	8,272,800	24,555,477.5	0.87	155.98	3.95	39.52	6.12	6.12
Primary diagnosis																
00 to 17 Years	35,004	35,004	154,919	5,014,716	10,136,053	14,744.2	0	0	23,075,999	57,191,897.6	1.52	143.26	4.43	32.37	0.00	0.00
18 to 44 Years	117,548	117,548	413,215	13,429,494	23,142,570	40,000.9	9	9	42,647,850	86,329,479.9	2.76	114.25	3.52	32.50	2.25	2.25
45 to 64 Years	48,996	48,996	202,330	7,255,317	12,577,916	21,175.0	3	3	26,255,503	66,469,346.6	1.87	148.08	4.13	35.86	1.42	1.42
65+ Years	7,222	7,222	28,504	1,126,455	2,083,677	3,268.2	2	2	8,273,042	24,557,577.9	0.87	155.98	3.95	39.52	6.12	6.12

Table 2: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Age Group

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member- Years	New Users/ 1K Eligible Members	Days Supplied / User	Dispensings/ User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
Levetiracetam																
7-day event washout																
Nonsecondary diagnosis																
00 to 17 Years	18,972	18,972	102,288	3,282,211	16,953,875	9,441.3	54	69	23,076,158	57,201,885.0	0.82	173.00	5.39	32.09	57.20	73.08
18 to 44 Years	27,268	27,268	91,686	2,874,459	7,779,813	8,526.8	46	54	42,655,922	86,397,983.1	0.64	105.42	3.36	31.35	53.95	63.33
45 to 64 Years	30,381	30,381	109,251	3,546,455	8,792,986	10,423.5	103	116	26,259,332	66,494,344.5	1.16	116.73	3.60	32.46	98.81	111.29
65+ Years	27,633	27,633	107,696	3,828,118	9,194,413	11,141.3	63	69	8,273,658	24,555,155.8	3.34	138.53	3.90	35.55	56.55	61.93
Primary diagnosis																
00 to 17 Years	18,976	18,976	102,316	3,282,996	16,957,173	9,444.8	40	51	23,076,158	57,201,919.0	0.82	173.01	5.39	32.09	42.35	54.00
18 to 44 Years	27,274	27,274	91,714	2,875,196	7,781,779	8,533.0	29	36	42,655,921	86,398,051.5	0.64	105.42	3.36	31.35	33.99	42.19
45 to 64 Years	30,406	30,406	109,334	3,548,748	8,797,747	10,436.7	52	53	26,259,332	66,494,483.0	1.16	116.71	3.60	32.46	49.82	50.78
65+ Years	27,643	27,643	107,760	3,829,937	9,198,202	11,149.5	32	34	8,273,661	24,555,268.6	3.34	138.55	3.90	35.54	28.70	30.49
183-day event washout																
Nonsecondary diagnosis																
00 to 17 Years	18,903	18,903	101,989	3,273,625	16,916,225	9,420.7	38	46	23,075,892	57,198,504.6	0.82	173.18	5.40	32.10	40.34	48.83
18 to 44 Years	27,189	27,189	91,491	2,869,088	7,763,907	8,510.9	40	46	42,655,516	86,394,287.8	0.64	105.52	3.37	31.36	47.00	54.05
45 to 64 Years	30,243	30,243	108,882	3,535,962	8,765,709	10,392.4	95	106	26,258,458	66,486,653.1	1.15	116.92	3.60	32.48	91.41	102.00
65+ Years	27,555	27,555	107,439	3,820,820	9,174,019	11,120.0	58	63	8,273,071	24,548,719.9	3.33	138.66	3.90	35.56	52.16	56.65
Primary diagnosis																
00 to 17 Years	18,926	18,926	102,120	3,277,592	16,928,450	9,432.8	29	36	23,075,999	57,199,240.7	0.82	173.18	5.40	32.10	30.74	38.16
18 to 44 Years	27,222	27,222	91,567	2,871,083	7,768,966	8,521.0	26	32	42,655,714	86,395,840.4	0.64	105.47	3.36	31.35	30.51	37.55
45 to 64 Years	30,325	30,325	109,115	3,542,781	8,785,412	10,419.1	47	47	26,258,840	66,489,588.1	1.15	116.83	3.60	32.47	45.11	45.11
65+ Years	27,601	27,601	107,658	3,827,075	9,191,728	11,140.9	29	30	8,273,310	24,550,798.8	3.34	138.66	3.90	35.55	26.03	26.93

Table 2: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Age Group

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member- Years	New Users/ 1K Eligible Members	Days Supplied / User	Dispensings/ User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
Topiramate																
<i>7-day event washout</i>																
Nonsecondary diagnosis																
00 to 17 Years	40,216	40,216	97,652	3,111,546	7,452,180	9,680.8	5	6	23,076,158	57,184,677.3	1.74	77.37	2.43	31.86	5.16	6.20
18 to 44 Years	220,947	220,947	549,076	17,841,626	39,694,080	55,038.1	13	16	42,644,799	86,232,762.0	5.18	80.75	2.49	32.49	2.36	2.91
45 to 64 Years	120,040	120,040	330,654	11,600,497	25,630,516	35,061.8	19	20	26,245,822	66,388,272.8	4.57	96.64	2.75	35.08	5.42	5.70
65+ Years	13,282	13,282	33,348	1,272,203	2,579,699	3,829.3	3	3	8,271,518	24,551,967.9	1.61	95.78	2.51	38.15	7.83	7.83
Primary diagnosis																
00 to 17 Years	40,217	40,217	97,654	3,111,618	7,452,484	9,681.1	4	5	23,076,158	57,184,714.2	1.74	77.37	2.43	31.86	4.13	5.16
18 to 44 Years	220,952	220,952	549,082	17,841,749	39,694,305	55,038.8	9	12	42,644,799	86,232,828.1	5.18	80.75	2.49	32.49	1.64	2.18
45 to 64 Years	120,044	120,044	330,658	11,600,617	25,630,726	35,063.9	13	14	26,245,822	66,388,415.0	4.57	96.64	2.75	35.08	3.71	3.99
65+ Years	13,282	13,282	33,348	1,272,203	2,579,699	3,829.3	3	3	8,271,521	24,552,081.4	1.61	95.78	2.51	38.15	7.83	7.83
<i>183-day event washout</i>																
Nonsecondary diagnosis																
00 to 17 Years	40,208	40,208	97,635	3,111,045	7,450,956	9,679.3	3	3	23,075,892	57,181,253.5	1.74	77.37	2.43	31.86	3.10	3.10
18 to 44 Years	220,919	220,919	549,019	17,839,887	39,690,398	55,032.9	12	13	42,644,389	86,229,068.0	5.18	80.75	2.49	32.49	2.18	2.36
45 to 64 Years	120,020	120,020	330,622	11,599,640	25,628,400	35,059.0	19	20	26,244,944	66,380,559.1	4.57	96.65	2.75	35.08	5.42	5.70
65+ Years	13,272	13,272	33,301	1,270,822	2,576,912	3,825.3	3	3	8,270,926	24,545,498.0	1.60	95.75	2.51	38.16	7.84	7.84
Primary diagnosis																
00 to 17 Years	40,211	40,211	97,641	3,111,230	7,451,426	9,679.9	2	2	23,075,999	57,181,998.3	1.74	77.37	2.43	31.86	2.07	2.07
18 to 44 Years	220,938	220,938	549,047	17,840,687	39,691,876	55,035.6	9	12	42,644,589	86,230,613.9	5.18	80.75	2.49	32.49	1.64	2.18
45 to 64 Years	120,035	120,035	330,643	11,600,235	25,629,822	35,062.7	13	14	26,245,325	66,383,508.1	4.57	96.64	2.75	35.08	3.71	3.99
65+ Years	13,276	13,276	33,305	1,270,913	2,577,093	3,825.6	3	3	8,271,168	24,547,595.8	1.61	95.73	2.51	38.16	7.84	7.84

Table 3: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Sex

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk
Carbamazepine																
7-day event washout																
Nonsecondary diagnosis																
Female	47,943	47,943	115,215	4,181,184	12,066,193	12,660.1	12	15	46,611,994	119,544,187.3	1.03	87.21	2.40	36.29	9.48	11.85
Male	34,297	34,297	99,067	3,635,556	12,121,096	10,867.0	10	12	45,458,551	114,991,998.5	0.75	106.00	2.89	36.70	9.20	11.04
Unknown	22	22	41	1,285	2,953	4.0	0	0	20,746	41,308.7	1.06	58.41	1.86	31.34	0.00	0.00
Primary diagnosis																
Female	47,944	47,944	115,216	4,181,194	12,066,213	12,661.4	6	9	46,611,996	119,544,362.2	1.03	87.21	2.40	36.29	4.74	7.11
Male	34,297	34,297	99,067	3,635,556	12,121,096	10,867.2	8	10	45,458,552	114,992,187.8	0.75	106.00	2.89	36.70	7.36	9.20
Unknown	22	22	41	1,285	2,953	4.0	0	0	20,746	41,308.7	1.06	58.41	1.86	31.34	0.00	0.00
183-day event washout																
Nonsecondary diagnosis																
Female	47,931	47,931	115,177	4,180,150	12,056,052	12,657.3	11	11	46,611,089	119,533,453.9	1.03	87.21	2.40	36.29	8.69	8.69
Male	34,286	34,286	99,050	3,635,097	12,119,686	10,865.7	8	10	45,457,616	114,981,405.3	0.75	106.02	2.89	36.70	7.36	9.20
Unknown	22	22	41	1,285	2,953	4.0	0	0	20,746	41,307.1	1.06	58.41	1.86	31.34	0.00	0.00
Primary diagnosis																
Female	47,934	47,934	115,183	4,180,280	12,056,672	12,659.0	5	5	46,611,488	119,537,150.1	1.03	87.21	2.40	36.29	3.95	3.95
Male	34,291	34,291	99,055	3,635,237	12,120,026	10,866.4	7	9	45,458,021	114,985,078.0	0.75	106.01	2.89	36.70	6.44	8.28
Unknown	22	22	41	1,285	2,953	4.0	0	0	20,746	41,307.1	1.06	58.41	1.86	31.34	0.00	0.00
Lamotrigine																
7-day event washout																
Nonsecondary diagnosis																
Female	135,688	135,688	498,981	16,692,666	29,993,443	49,401.6	17	18	46,612,021	119,525,587.6	2.91	123.02	3.68	33.45	3.44	3.64
Male	73,018	73,018	299,799	10,127,557	17,937,856	29,765.9	8	8	45,458,558	114,995,376.7	1.61	138.70	4.11	33.78	2.69	2.69
Unknown	75	75	216	6,573	10,496	19.1	0	0	20,746	41,321.7	3.62	87.64	2.88	30.43	0.00	0.00
Primary diagnosis																
Female	135,690	135,690	498,983	16,692,726	29,993,533	49,404.8	10	10	46,612,023	119,525,762.1	2.91	123.02	3.68	33.45	2.02	2.02
Male	73,019	73,019	299,801	10,127,617	17,937,901	29,767.2	4	4	45,458,559	114,995,565.1	1.61	138.70	4.11	33.78	1.34	1.34
Unknown	75	75	216	6,573	10,496	19.1	0	0	20,746	41,321.7	3.62	87.64	2.88	30.43	0.00	0.00
183-day event washout																
Nonsecondary diagnosis																
Female	135,676	135,676	498,963	16,692,115	29,992,553	49,400.1	15	16	46,611,116	119,514,845.3	2.91	123.03	3.68	33.45	3.04	3.24
Male	73,011	73,011	299,773	10,126,839	17,936,592	29,763.8	8	8	45,457,623	114,984,763.2	1.61	138.70	4.11	33.78	2.69	2.69
Unknown	75	75	216	6,573	10,496	19.1	0	0	20,746	41,320.2	3.62	87.64	2.88	30.43	0.00	0.00
Primary diagnosis																
Female	135,682	135,682	498,971	16,692,344	29,992,840	49,403.5	10	10	46,611,515	119,518,540.8	2.91	123.03	3.68	33.45	2.02	2.02
Male	73,013	73,013	299,781	10,127,065	17,936,879	29,765.6	4	4	45,458,028	114,988,441.0	1.61	138.70	4.11	33.78	1.34	1.34
Unknown	75	75	216	6,573	10,496	19.1	0	0	20,746	41,320.2	3.62	87.64	2.88	30.43	0.00	0.00

Table 3: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Sex

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk
Levetiracetam																
7-day event washout																
Nonsecondary diagnosis																
Female	53,462	53,462	206,388	6,773,730	20,999,991	19,815.1	128	141	46,612,021	119,590,203.4	1.15	126.70	3.86	32.82	64.60	71.16
Male	50,763	50,763	204,411	6,753,937	21,709,960	19,707.4	138	167	45,458,558	115,017,832.2	1.12	133.05	4.03	33.04	70.02	84.74
Unknown	29	29	122	3,576	11,135	10.4	0	0	20,746	41,332.8	1.40	123.31	4.21	29.31	0.00	0.00
Primary diagnosis																
Female	53,486	53,486	206,442	6,775,115	21,003,628	19,825.3	77	85	46,612,023	119,590,370.6	1.15	126.67	3.86	32.82	38.84	42.87
Male	50,784	50,784	204,560	6,758,186	21,720,137	19,728.3	76	89	45,458,559	115,018,018.8	1.12	133.08	4.03	33.04	38.52	45.11
Unknown	29	29	122	3,576	11,135	10.4	0	0	20,746	41,332.8	1.40	123.31	4.21	29.31	0.00	0.00
183-day event washout																
Nonsecondary diagnosis																
Female	53,285	53,285	205,790	6,756,500	20,947,804	19,766.8	112	120	46,611,116	119,579,531.9	1.14	126.80	3.86	32.83	56.66	60.71
Male	50,577	50,577	203,890	6,739,448	21,660,979	19,666.9	119	141	45,457,623	115,007,302.2	1.11	133.25	4.03	33.05	60.51	71.69
Unknown	28	28	121	3,547	11,077	10.4	0	0	20,746	41,331.3	1.35	126.68	4.32	29.31	0.00	0.00
Primary diagnosis																
Female	53,374	53,374	206,087	6,764,960	20,968,493	19,797.1	67	73	46,611,515	119,583,194.1	1.15	126.75	3.86	32.83	33.84	36.87
Male	50,672	50,672	204,252	6,750,024	21,694,985	19,706.3	64	72	45,458,028	115,010,942.6	1.11	133.21	4.03	33.05	32.48	36.54
Unknown	28	28	121	3,547	11,077	10.4	0	0	20,746	41,331.3	1.35	126.68	4.32	29.31	0.00	0.00
Topiramate																
7-day event washout																
Nonsecondary diagnosis																
Female	319,403	319,403	835,135	27,995,245	61,995,938	85,591.9	29	31	46,612,021	119,345,073.8	6.85	87.65	2.61	33.52	3.39	3.62
Male	74,967	74,967	175,408	5,825,289	13,346,669	18,001.4	11	14	45,458,558	114,971,307.4	1.65	77.70	2.34	33.21	6.11	7.78
Unknown	115	115	187	5,338	13,868	16.8	0	0	20,746	41,298.9	5.54	46.42	1.63	28.55	0.00	0.00
Primary diagnosis																
Female	319,413	319,413	835,147	27,995,560	61,996,677	85,594.9	20	22	46,612,023	119,345,243.1	6.85	87.65	2.61	33.52	2.34	2.57
Male	74,967	74,967	175,408	5,825,289	13,346,669	18,001.5	9	12	45,458,559	114,971,496.7	1.65	77.70	2.34	33.21	5.00	6.67
Unknown	115	115	187	5,338	13,868	16.8	0	0	20,746	41,298.9	5.54	46.42	1.63	28.55	0.00	0.00
183-day event washout																
Nonsecondary diagnosis																
Female	319,349	319,349	835,001	27,991,292	61,987,534	85,579.9	28	28	46,611,116	119,334,375.4	6.85	87.65	2.61	33.52	3.27	3.27
Male	74,955	74,955	175,389	5,824,764	13,345,264	17,999.8	9	11	45,457,623	114,960,705.8	1.65	77.71	2.34	33.21	5.00	6.11
Unknown	115	115	187	5,338	13,868	16.8	0	0	20,746	41,297.3	5.54	46.42	1.63	28.55	0.00	0.00
Primary diagnosis																
Female	319,382	319,382	835,046	27,992,589	61,990,158	85,585.9	20	22	46,611,515	119,338,038.9	6.85	87.65	2.61	33.52	2.34	2.57
Male	74,963	74,963	175,403	5,825,138	13,346,191	18,001.1	7	9	45,458,028	114,964,379.8	1.65	77.71	2.34	33.21	3.89	5.00
Unknown	115	115	187	5,338	13,868	16.8	0	0	20,746	41,297.3	5.54	46.42	1.63	28.55	0.00	0.00

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
Carbamazepine																
<i>7-day event washout</i>																
Nonsecondary diagnosis																
2000	2,880	2,880	8,450	332,634	1,113,327	989.7	1	1	7,045,322	3,216,544.6	0.41	115.50	2.93	39.36	10.10	10.10
2001	5,404	5,404	17,113	649,369	2,078,864	1,926.0	0	0	7,642,185	6,359,709.8	0.71	120.16	3.17	37.95	0.00	0.00
2002	4,673	4,673	13,894	569,813	1,796,262	1,683.3	1	1	7,765,602	6,425,059.7	0.60	121.94	2.97	41.01	5.94	5.94
2003	4,171	4,171	14,139	576,236	2,113,044	1,687.6	1	1	7,687,524	6,344,242.5	0.54	138.15	3.39	40.76	5.93	5.93
2004	3,791	3,791	10,706	449,252	2,079,736	1,327.7	0	0	8,197,617	6,511,342.4	0.46	118.50	2.82	41.96	0.00	0.00
2005	3,656	3,656	10,029	429,219	1,409,359	1,266.9	1	1	8,443,223	6,859,437.5	0.43	117.40	2.74	42.80	7.89	7.89
2006	4,678	4,678	14,545	565,978	1,690,850	1,675.6	1	1	19,129,517	11,511,036.3	0.24	120.99	3.11	38.91	5.97	5.97
2007	5,561	5,561	15,037	559,337	1,634,575	1,679.2	0	0	22,779,017	16,364,011.2	0.24	100.58	2.70	37.20	0.00	0.00
2008	8,336	8,336	20,899	739,490	2,168,319	2,240.3	4	7	43,384,052	26,936,844.4	0.19	88.71	2.51	35.38	17.85	31.25
2009	10,000	10,000	24,306	819,275	2,304,132	2,509.0	4	4	45,237,006	34,578,676.0	0.22	81.93	2.43	33.71	15.94	15.94
2010	9,219	9,219	22,284	740,910	2,094,009	2,268.5	2	2	43,430,981	33,345,009.5	0.21	80.37	2.42	33.25	8.82	8.82
2011	8,627	8,627	20,372	676,228	1,854,302	2,072.4	4	6	42,267,033	32,760,400.1	0.20	78.39	2.36	33.19	19.30	28.95
2012	8,301	8,301	17,651	567,489	1,474,078	1,756.0	2	2	41,140,723	31,582,776.0	0.20	68.36	2.13	32.15	11.39	11.39
2013	2,965	2,965	4,898	142,795	379,386	448.9	1	1	31,670,126	11,782,404.4	0.09	48.16	1.65	29.15	22.28	22.28
Primary diagnosis																
2000	2,880	2,880	8,450	332,634	1,113,327	989.7	1	1	7,045,322	3,216,544.6	0.41	115.50	2.93	39.36	10.10	10.10
2001	5,404	5,404	17,113	649,369	2,078,864	1,926.0	0	0	7,642,185	6,359,709.8	0.71	120.16	3.17	37.95	0.00	0.00
2002	4,673	4,673	13,894	569,813	1,796,262	1,683.3	1	1	7,765,602	6,425,059.7	0.60	121.94	2.97	41.01	5.94	5.94
2003	4,171	4,171	14,139	576,236	2,113,044	1,687.6	1	1	7,687,524	6,344,242.5	0.54	138.15	3.39	40.76	5.93	5.93
2004	3,791	3,791	10,706	449,252	2,079,736	1,327.7	0	0	8,197,617	6,511,342.4	0.46	118.50	2.82	41.96	0.00	0.00
2005	3,656	3,656	10,029	429,219	1,409,359	1,266.9	1	1	8,443,223	6,859,438.2	0.43	117.40	2.74	42.80	7.89	7.89
2006	4,678	4,678	14,545	565,978	1,690,850	1,675.6	1	1	19,129,518	11,511,041.3	0.24	120.99	3.11	38.91	5.97	5.97
2007	5,561	5,561	15,037	559,337	1,634,575	1,679.2	0	0	22,779,018	16,364,021.0	0.24	100.58	2.70	37.20	0.00	0.00
2008	8,336	8,336	20,899	739,490	2,168,319	2,241.3	2	5	43,384,055	26,936,887.4	0.19	88.71	2.51	35.38	8.92	22.31
2009	10,000	10,000	24,306	819,275	2,304,132	2,509.2	1	1	45,237,012	34,578,752.8	0.22	81.93	2.43	33.71	3.99	3.99
2010	9,220	9,220	22,285	740,920	2,094,029	2,268.6	1	1	43,430,983	33,345,076.1	0.21	80.36	2.42	33.25	4.41	4.41
2011	8,627	8,627	20,372	676,228	1,854,302	2,072.4	4	6	42,267,033	32,760,465.5	0.20	78.39	2.36	33.19	19.30	28.95
2012	8,301	8,301	17,651	567,489	1,474,078	1,756.1	1	1	41,140,724	31,582,844.1	0.20	68.36	2.13	32.15	5.69	5.69
2013	2,965	2,965	4,898	142,795	379,386	449.0	0	0	31,670,128	11,782,433.4	0.09	48.16	1.65	29.15	0.00	0.00

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
183-day event washout																
Nonsecondary diagnosis																
2000	2,878	2,878	8,448	332,504	1,112,947	989.4	0	0	7,045,228	3,216,422.8	0.41	115.53	2.94	39.36	0.00	0.00
2001	5,403	5,403	17,112	649,403	2,078,590	1,926.1	0	0	7,642,113	6,359,481.7	0.71	120.19	3.17	37.95	0.00	0.00
2002	4,671	4,671	13,891	569,728	1,796,117	1,683.0	1	1	7,765,540	6,424,821.3	0.60	121.97	2.97	41.01	5.94	5.94
2003	4,170	4,170	14,138	576,206	2,112,954	1,687.5	1	1	7,687,468	6,344,040.7	0.54	138.18	3.39	40.76	5.93	5.93
2004	3,788	3,788	10,701	449,128	2,079,296	1,327.4	0	0	8,197,548	6,511,122.4	0.46	118.57	2.82	41.97	0.00	0.00
2005	3,656	3,656	10,029	429,219	1,409,359	1,266.9	1	1	8,443,164	6,859,207.7	0.43	117.40	2.74	42.80	7.89	7.89
2006	4,678	4,678	14,545	565,978	1,690,850	1,675.6	1	1	19,128,992	11,510,192.3	0.24	120.99	3.11	38.91	5.97	5.97
2007	5,561	5,561	15,037	559,337	1,634,575	1,679.2	0	0	22,778,367	16,362,576.4	0.24	100.58	2.70	37.20	0.00	0.00
2008	8,334	8,334	20,877	738,841	2,159,574	2,238.8	3	3	43,382,671	26,934,105.9	0.19	88.65	2.51	35.39	13.40	13.40
2009	9,996	9,996	24,302	819,166	2,303,791	2,508.7	3	3	45,235,728	34,575,012.9	0.22	81.95	2.43	33.71	11.96	11.96
2010	9,214	9,214	22,276	740,739	2,093,300	2,268.0	2	2	43,429,850	33,341,645.4	0.21	80.39	2.42	33.25	8.82	8.82
2011	8,627	8,627	20,372	676,228	1,854,302	2,072.4	4	6	42,265,880	32,757,025.5	0.20	78.39	2.36	33.19	19.30	28.95
2012	8,300	8,300	17,650	567,469	1,474,038	1,755.9	2	2	41,139,594	31,579,390.8	0.20	68.37	2.13	32.15	11.39	11.39
2013	2,963	2,963	4,890	142,586	378,998	448.3	1	1	31,668,562	11,781,120.6	0.09	48.12	1.65	29.16	22.31	22.31
Primary diagnosis																
2000	2,878	2,878	8,448	332,504	1,112,947	989.4	0	0	7,045,228	3,216,422.8	0.41	115.53	2.94	39.36	0.00	0.00
2001	5,403	5,403	17,112	649,403	2,078,590	1,926.1	0	0	7,642,113	6,359,482.1	0.71	120.19	3.17	37.95	0.00	0.00
2002	4,671	4,671	13,891	569,728	1,796,117	1,683.0	1	1	7,765,540	6,424,821.3	0.60	121.97	2.97	41.01	5.94	5.94
2003	4,170	4,170	14,138	576,206	2,112,954	1,687.5	1	1	7,687,468	6,344,040.7	0.54	138.18	3.39	40.76	5.93	5.93
2004	3,788	3,788	10,701	449,128	2,079,296	1,327.4	0	0	8,197,548	6,511,122.5	0.46	118.57	2.82	41.97	0.00	0.00
2005	3,656	3,656	10,029	429,219	1,409,359	1,266.9	1	1	8,443,164	6,859,221.9	0.43	117.40	2.74	42.80	7.89	7.89
2006	4,678	4,678	14,545	565,978	1,690,850	1,675.6	1	1	19,129,068	11,510,294.8	0.24	120.99	3.11	38.91	5.97	5.97
2007	5,561	5,561	15,037	559,337	1,634,575	1,679.2	0	0	22,778,411	16,362,760.8	0.24	100.58	2.70	37.20	0.00	0.00
2008	8,335	8,335	20,878	738,871	2,159,634	2,239.8	1	1	43,383,341	26,935,013.8	0.19	88.65	2.50	35.39	4.46	4.46
2009	9,998	9,998	24,304	819,226	2,303,971	2,509.1	1	1	45,236,301	34,576,574.6	0.22	81.94	2.43	33.71	3.99	3.99
2010	9,218	9,218	22,283	740,899	2,093,980	2,268.6	1	1	43,430,328	33,343,060.1	0.21	80.38	2.42	33.25	4.41	4.41
2011	8,627	8,627	20,372	676,228	1,854,302	2,072.4	4	6	42,266,289	32,758,298.4	0.20	78.39	2.36	33.19	19.30	28.95
2012	8,301	8,301	17,651	567,489	1,474,078	1,756.1	1	1	41,140,046	31,580,743.0	0.20	68.36	2.13	32.15	5.69	5.69
2013	2,963	2,963	4,890	142,586	378,998	448.4	0	0	31,669,177	11,781,678.5	0.09	48.12	1.65	29.16	0.00	0.00

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Days Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
Lamotrigine																
<i>7-day event washout</i>																
Nonsecondary diagnosis																
2000	217	217	727	30,797	65,228	89.8	0	0	7,045,322	3,216,544.6	0.03	141.92	3.35	42.36	0.00	0.00
2001	655	655	2,343	95,079	229,766	277.0	0	0	7,643,625	6,360,580.0	0.09	145.16	3.58	40.58	0.00	0.00
2002	968	968	4,219	192,022	451,462	551.9	0	0	7,769,994	6,428,100.9	0.12	198.37	4.36	45.51	0.00	0.00
2003	2,324	2,324	9,711	378,824	921,644	1,102.0	0	0	7,693,802	6,348,689.0	0.30	163.01	4.18	39.01	0.00	0.00
2004	4,022	4,022	17,143	635,501	1,932,414	1,853.3	0	0	8,204,690	6,516,712.3	0.49	158.01	4.26	37.07	0.00	0.00
2005	4,991	4,991	20,111	745,629	1,478,979	2,182.6	0	0	8,450,237	6,865,048.5	0.59	149.39	4.03	37.08	0.00	0.00
2006	10,871	10,871	49,135	1,797,349	3,286,036	5,237.7	1	1	19,135,320	11,515,899.2	0.57	165.33	4.52	36.58	1.91	1.91
2007	16,300	16,300	72,224	2,560,685	4,427,511	7,496.7	3	3	22,782,706	16,367,815.9	0.72	157.10	4.43	35.45	4.00	4.00
2008	28,386	28,386	118,707	3,989,219	6,854,012	11,756.0	3	3	43,383,784	26,938,148.4	0.65	140.53	4.18	33.61	2.55	2.55
2009	34,356	34,356	136,927	4,535,842	7,840,410	13,409.5	4	4	45,230,222	34,576,092.9	0.76	132.02	3.99	33.13	2.98	2.98
2010	31,921	31,921	125,899	4,168,434	7,217,292	12,317.4	4	4	43,416,544	33,337,108.6	0.74	130.59	3.94	33.11	3.25	3.25
2011	31,697	31,697	118,818	3,879,239	6,603,559	11,486.5	6	7	42,246,189	32,747,778.5	0.75	122.39	3.75	32.65	5.22	6.09
2012	30,991	30,991	97,878	3,090,496	5,338,716	9,227.4	4	4	41,114,882	31,566,500.8	0.75	99.72	3.16	31.57	4.33	4.33
2013	11,082	11,082	25,154	727,680	1,294,766	2,198.8	0	0	31,653,930	11,777,266.5	0.35	65.66	2.27	28.93	0.00	0.00
Primary diagnosis																
2000	217	217	727	30,797	65,228	89.8	0	0	7,045,322	3,216,544.6	0.03	141.92	3.35	42.36	0.00	0.00
2001	655	655	2,343	95,079	229,766	277.0	0	0	7,643,625	6,360,580.0	0.09	145.16	3.58	40.58	0.00	0.00
2002	968	968	4,219	192,022	451,462	551.9	0	0	7,769,994	6,428,100.9	0.12	198.37	4.36	45.51	0.00	0.00
2003	2,324	2,324	9,711	378,824	921,644	1,102.0	0	0	7,693,802	6,348,689.0	0.30	163.01	4.18	39.01	0.00	0.00
2004	4,022	4,022	17,143	635,501	1,932,414	1,853.3	0	0	8,204,690	6,516,712.3	0.49	158.01	4.26	37.07	0.00	0.00
2005	4,991	4,991	20,111	745,629	1,478,979	2,182.6	0	0	8,450,237	6,865,049.2	0.59	149.39	4.03	37.08	0.00	0.00
2006	10,871	10,871	49,135	1,797,349	3,286,036	5,237.7	1	1	19,135,321	11,515,904.1	0.57	165.33	4.52	36.58	1.91	1.91
2007	16,300	16,300	72,224	2,560,685	4,427,511	7,496.7	3	3	22,782,707	16,367,825.7	0.72	157.10	4.43	35.45	4.00	4.00
2008	28,386	28,386	118,707	3,989,219	6,854,012	11,756.2	1	1	43,383,787	26,938,191.4	0.65	140.53	4.18	33.61	0.85	0.85
2009	34,356	34,356	136,927	4,535,842	7,840,410	13,410.1	2	2	45,230,228	34,576,169.6	0.76	132.02	3.99	33.13	1.49	1.49
2010	31,921	31,921	125,899	4,168,434	7,217,292	12,317.5	2	2	43,416,546	33,337,175.2	0.74	130.59	3.94	33.11	1.62	1.62
2011	31,698	31,698	118,820	3,879,299	6,603,604	11,488.8	3	3	42,246,189	32,747,843.7	0.75	122.38	3.75	32.65	2.61	2.61
2012	30,993	30,993	97,880	3,090,556	5,338,806	9,228.7	2	2	41,114,882	31,566,568.1	0.75	99.72	3.16	31.57	2.17	2.17
2013	11,082	11,082	25,154	727,680	1,294,766	2,198.8	0	0	31,653,929	11,777,295.0	0.35	65.66	2.27	28.93	0.00	0.00

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
183-day event washout																
Nonsecondary diagnosis																
2000	217	217	727	30,797	65,228	89.8	0	0	7,045,228	3,216,422.8	0.03	141.92	3.35	42.36	0.00	0.00
2001	655	655	2,343	95,079	229,766	277.0	0	0	7,643,552	6,360,351.8	0.09	145.16	3.58	40.58	0.00	0.00
2002	968	968	4,219	192,022	451,462	551.9	0	0	7,769,930	6,427,860.1	0.12	198.37	4.36	45.51	0.00	0.00
2003	2,324	2,324	9,711	378,824	921,644	1,102.0	0	0	7,693,741	6,348,484.1	0.30	163.01	4.18	39.01	0.00	0.00
2004	4,022	4,022	17,143	635,501	1,932,414	1,853.3	0	0	8,204,616	6,516,487.4	0.49	158.01	4.26	37.07	0.00	0.00
2005	4,991	4,991	20,111	745,629	1,478,979	2,182.6	0	0	8,450,171	6,864,814.6	0.59	149.39	4.03	37.08	0.00	0.00
2006	10,870	10,870	49,134	1,797,281	3,285,931	5,237.5	1	1	19,134,791	11,515,051.6	0.57	165.34	4.52	36.58	1.91	1.91
2007	16,298	16,298	72,222	2,560,640	4,427,421	7,496.5	3	3	22,782,053	16,366,379.6	0.72	157.11	4.43	35.46	4.00	4.00
2008	28,383	28,383	118,703	3,989,119	6,853,862	11,755.7	3	3	43,382,404	26,935,408.9	0.65	140.55	4.18	33.61	2.55	2.55
2009	34,353	34,353	136,923	4,535,761	7,840,215	13,409.3	4	4	45,228,945	34,572,430.2	0.76	132.03	3.99	33.13	2.98	2.98
2010	31,918	31,918	125,889	4,168,141	7,216,946	12,316.5	4	4	43,415,414	33,333,741.7	0.74	130.59	3.94	33.11	3.25	3.25
2011	31,692	31,692	118,811	3,879,023	6,603,253	11,486.1	4	5	42,245,028	32,744,399.0	0.75	122.40	3.75	32.65	3.48	4.35
2012	30,990	30,990	97,868	3,090,196	5,337,996	9,226.6	4	4	41,113,753	31,563,114.8	0.75	99.72	3.16	31.58	4.34	4.34
2013	11,081	11,081	25,148	727,514	1,294,524	2,198.3	0	0	31,652,366	11,775,982.2	0.35	65.65	2.27	28.93	0.00	0.00
Primary diagnosis																
2000	217	217	727	30,797	65,228	89.8	0	0	7,045,228	3,216,422.8	0.03	141.92	3.35	42.36	0.00	0.00
2001	655	655	2,343	95,079	229,766	277.0	0	0	7,643,552	6,360,352.1	0.09	145.16	3.58	40.58	0.00	0.00
2002	968	968	4,219	192,022	451,462	551.9	0	0	7,769,930	6,427,860.1	0.12	198.37	4.36	45.51	0.00	0.00
2003	2,324	2,324	9,711	378,824	921,644	1,102.0	0	0	7,693,741	6,348,484.1	0.30	163.01	4.18	39.01	0.00	0.00
2004	4,022	4,022	17,143	635,501	1,932,414	1,853.3	0	0	8,204,616	6,516,487.4	0.49	158.01	4.26	37.07	0.00	0.00
2005	4,991	4,991	20,111	745,629	1,478,979	2,182.6	0	0	8,450,175	6,864,828.8	0.59	149.39	4.03	37.08	0.00	0.00
2006	10,870	10,870	49,134	1,797,281	3,285,931	5,237.5	1	1	19,134,867	11,515,154.1	0.57	165.34	4.52	36.58	1.91	1.91
2007	16,298	16,298	72,222	2,560,640	4,427,421	7,496.5	3	3	22,782,097	16,366,563.7	0.72	157.11	4.43	35.46	4.00	4.00
2008	28,384	28,384	118,704	3,989,149	6,853,897	11,755.9	1	1	43,383,074	26,936,316.8	0.65	140.54	4.18	33.61	0.85	0.85
2009	34,354	34,354	136,924	4,535,771	7,840,248	13,409.9	2	2	45,229,517	34,573,990.7	0.76	132.03	3.99	33.13	1.49	1.49
2010	31,918	31,918	125,889	4,168,141	7,216,946	12,316.6	2	2	43,415,894	33,335,158.3	0.74	130.59	3.94	33.11	1.62	1.62
2011	31,695	31,695	118,817	3,879,212	6,603,427	11,488.5	3	3	42,245,444	32,745,675.7	0.75	122.39	3.75	32.65	2.61	2.61
2012	30,992	30,992	97,870	3,090,256	5,338,086	9,227.8	2	2	41,114,206	31,564,466.6	0.75	99.71	3.16	31.58	2.17	2.17
2013	11,082	11,082	25,154	727,680	1,294,766	2,198.8	0	0	31,652,979	11,776,540.6	0.35	65.66	2.27	28.93	0.00	0.00

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
Levetiracetam																
<i>7-day event washout</i>																
Nonsecondary diagnosis																
2000	28	28	91	3,658	8,623	10.8	0	0	7,045,322	3,216,544.6	0.00	130.64	3.25	40.20	0.00	0.00
2001	185	185	500	14,376	35,501	44.4	0	0	7,643,694	6,360,610.3	0.02	77.71	2.70	28.75	0.00	0.00
2002	328	328	1,120	37,926	92,940	112.9	0	0	7,770,245	6,428,241.9	0.04	115.63	3.41	33.86	0.00	0.00
2003	970	970	3,681	117,376	551,087	348.1	0	0	7,694,300	6,348,996.3	0.13	121.01	3.79	31.89	0.00	0.00
2004	1,227	1,227	4,740	158,649	828,002	467.6	1	1	8,205,704	6,517,338.3	0.15	129.30	3.86	33.47	21.38	21.38
2005	1,321	1,321	5,492	190,842	850,906	558.1	0	0	8,452,370	6,866,337.3	0.16	144.47	4.16	34.75	0.00	0.00
2006	2,733	2,733	13,709	492,156	1,780,049	1,421.8	4	4	19,138,931	11,518,205.2	0.14	180.08	5.02	35.90	28.13	28.13
2007	5,114	5,114	24,716	844,413	2,756,462	2,447.6	14	15	22,789,350	16,372,045.0	0.22	165.12	4.83	34.16	57.20	61.28
2008	10,865	10,865	50,685	1,703,696	5,215,732	4,946.4	36	41	43,394,912	26,945,297.3	0.25	156.81	4.66	33.61	72.78	82.89
2009	16,537	16,537	75,567	2,485,835	7,741,504	7,229.3	47	53	45,247,565	34,586,893.0	0.37	150.32	4.57	32.90	65.01	73.31
2010	17,447	17,447	75,133	2,487,377	7,551,822	7,245.1	42	51	43,440,025	33,352,330.2	0.40	142.57	4.31	33.11	57.97	70.39
2011	19,232	19,232	73,811	2,469,628	7,577,007	7,223.4	50	58	42,274,148	32,766,479.2	0.45	128.41	3.84	33.46	69.22	80.29
2012	20,522	20,522	65,170	2,060,932	6,472,118	6,085.1	53	64	41,145,129	31,586,889.1	0.50	100.43	3.18	31.62	87.10	105.17
2013	7,745	7,745	16,506	464,379	1,259,333	1,392.2	19	21	31,671,557	11,783,160.7	0.24	59.96	2.13	28.13	136.48	150.84
Primary diagnosis																
2000	28	28	91	3,658	8,623	10.8	0	0	7,045,322	3,216,544.6	0.00	130.64	3.25	40.20	0.00	0.00
2001	185	185	500	14,376	35,501	44.4	0	0	7,643,694	6,360,610.3	0.02	77.71	2.70	28.75	0.00	0.00
2002	328	328	1,120	37,926	92,940	112.9	0	0	7,770,245	6,428,241.9	0.04	115.63	3.41	33.86	0.00	0.00
2003	970	970	3,681	117,376	551,087	348.1	0	0	7,694,300	6,348,996.3	0.13	121.01	3.79	31.89	0.00	0.00
2004	1,227	1,227	4,740	158,649	828,002	467.6	1	1	8,205,704	6,517,338.3	0.15	129.30	3.86	33.47	21.38	21.38
2005	1,321	1,321	5,492	190,842	850,906	558.1	0	0	8,452,370	6,866,338.0	0.16	144.47	4.16	34.75	0.00	0.00
2006	2,733	2,733	13,709	492,156	1,780,049	1,421.9	3	3	19,138,932	11,518,210.1	0.14	180.08	5.02	35.90	21.10	21.10
2007	5,114	5,114	24,716	844,413	2,756,462	2,448.5	12	12	22,789,351	16,372,054.8	0.22	165.12	4.83	34.16	49.01	49.01
2008	10,872	10,872	50,699	1,704,074	5,216,518	4,948.5	25	30	43,394,915	26,945,340.3	0.25	156.74	4.66	33.61	50.52	60.62
2009	16,542	16,542	75,639	2,487,908	7,746,938	7,237.2	25	30	45,247,571	34,586,969.8	0.37	150.40	4.57	32.89	34.54	41.45
2010	17,456	17,456	75,170	2,488,425	7,553,888	7,252.6	24	26	43,440,027	33,352,396.7	0.40	142.55	4.31	33.10	33.09	35.85
2011	19,245	19,245	73,857	2,470,894	7,580,429	7,229.4	34	38	42,274,145	32,766,543.6	0.46	128.39	3.84	33.46	47.03	52.56
2012	20,529	20,529	65,187	2,061,377	6,473,188	6,089.7	21	26	41,145,121	31,586,950.6	0.50	100.41	3.18	31.62	34.48	42.69
2013	7,749	7,749	16,523	464,803	1,260,369	1,394.2	8	8	31,671,552	11,783,186.8	0.24	59.98	2.13	28.13	57.38	57.38

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk
183-day event washout																
Nonsecondary diagnosis																
2000	28	28	91	3,658	8,623	10.8	0	0	7,045,228	3,216,422.8	0.00	130.64	3.25	40.20	0.00	0.00
2001	184	184	499	14,367	35,483	44.3	0	0	7,643,621	6,360,382.0	0.02	78.08	2.71	28.79	0.00	0.00
2002	327	327	1,119	37,906	92,900	112.8	0	0	7,770,181	6,428,001.3	0.04	115.92	3.42	33.87	0.00	0.00
2003	968	968	3,671	117,076	550,487	347.3	0	0	7,694,241	6,348,792.7	0.13	120.95	3.79	31.89	0.00	0.00
2004	1,227	1,227	4,740	158,649	828,002	467.6	1	1	8,205,632	6,517,114.5	0.15	129.30	3.86	33.47	21.38	21.38
2005	1,321	1,321	5,492	190,842	850,906	558.1	0	0	8,452,303	6,866,103.7	0.16	144.47	4.16	34.75	0.00	0.00
2006	2,728	2,728	13,684	491,313	1,777,737	1,419.3	3	3	19,138,402	11,517,357.3	0.14	180.10	5.02	35.90	21.14	21.14
2007	5,099	5,099	24,657	842,775	2,750,376	2,443.3	10	11	22,788,695	16,370,607.3	0.22	165.28	4.84	34.18	40.93	45.02
2008	10,823	10,823	50,540	1,699,211	5,203,171	4,933.5	30	33	43,393,538	26,942,563.2	0.25	157.00	4.67	33.62	60.81	66.89
2009	16,463	16,463	75,370	2,480,584	7,728,130	7,213.9	41	46	45,246,306	34,583,240.1	0.36	150.68	4.58	32.91	56.84	63.77
2010	17,389	17,389	74,941	2,481,525	7,539,214	7,227.8	41	49	43,438,930	33,348,984.4	0.40	142.71	4.31	33.11	56.73	67.79
2011	19,162	19,162	73,540	2,462,011	7,552,003	7,204.4	43	47	42,273,046	32,763,138.9	0.45	128.48	3.84	33.48	59.69	65.24
2012	20,446	20,446	64,975	2,055,729	6,444,792	6,070.4	44	51	41,144,070	31,583,558.4	0.50	100.54	3.18	31.64	72.48	84.01
2013	7,725	7,725	16,482	463,849	1,258,035	1,390.5	18	20	31,670,055	11,781,898.8	0.24	60.05	2.13	28.14	129.45	143.83
Primary diagnosis																
2000	28	28	91	3,658	8,623	10.8	0	0	7,045,228	3,216,422.8	0.00	130.64	3.25	40.20	0.00	0.00
2001	184	184	499	14,367	35,483	44.3	0	0	7,643,621	6,360,382.4	0.02	78.08	2.71	28.79	0.00	0.00
2002	327	327	1,119	37,906	92,900	112.8	0	0	7,770,181	6,428,001.3	0.04	115.92	3.42	33.87	0.00	0.00
2003	968	968	3,671	117,076	550,487	347.3	0	0	7,694,241	6,348,792.7	0.13	120.95	3.79	31.89	0.00	0.00
2004	1,227	1,227	4,740	158,649	828,002	467.6	1	1	8,205,632	6,517,114.5	0.15	129.30	3.86	33.47	21.38	21.38
2005	1,321	1,321	5,492	190,842	850,906	558.1	0	0	8,452,307	6,866,117.9	0.16	144.47	4.16	34.75	0.00	0.00
2006	2,728	2,728	13,684	491,313	1,777,737	1,419.4	2	2	19,138,478	11,517,459.8	0.14	180.10	5.02	35.90	14.09	14.09
2007	5,100	5,100	24,663	842,955	2,750,736	2,444.7	8	8	22,788,739	16,370,791.6	0.22	165.29	4.84	34.18	32.72	32.72
2008	10,847	10,847	50,645	1,702,498	5,211,848	4,944.0	20	23	43,394,207	26,943,470.4	0.25	156.96	4.67	33.62	40.45	46.52
2009	16,494	16,494	75,505	2,484,370	7,737,194	7,226.8	22	26	45,246,873	34,584,797.4	0.36	150.62	4.58	32.90	30.44	35.98
2010	17,422	17,422	75,069	2,485,523	7,547,366	7,243.9	24	26	43,439,395	33,350,393.0	0.40	142.67	4.31	33.11	33.13	35.89
2011	19,200	19,200	73,677	2,465,786	7,560,543	7,217.6	28	30	42,273,431	32,764,396.5	0.45	128.43	3.84	33.47	38.79	41.56
2012	20,486	20,486	65,091	2,058,970	6,462,809	6,083.0	19	22	41,144,482	31,584,880.8	0.50	100.51	3.18	31.63	31.23	36.17
2013	7,742	7,742	16,514	464,618	1,259,921	1,393.6	7	7	31,670,642	11,782,446.8	0.24	60.01	2.13	28.13	50.23	50.23

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Days Dispensings	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Days Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
Topiramate																
<i>7-day event washout</i>																
Nonsecondary diagnosis																
2000	549	549	1,814	64,137	192,109	190.8	0	0	7,045,322	3,216,544.6	0.08	116.83	3.30	35.36	0.00	0.00
2001	2,146	2,146	6,042	212,142	546,019	639.4	1	1	7,643,433	6,360,440.0	0.28	98.85	2.82	35.11	15.64	15.64
2002	3,775	3,775	12,064	469,199	1,121,523	1,391.0	0	0	7,768,829	6,427,334.6	0.49	124.29	3.20	38.89	0.00	0.00
2003	7,851	7,851	25,569	906,812	2,436,774	2,704.7	0	0	7,691,118	6,347,011.5	1.02	115.50	3.26	35.47	0.00	0.00
2004	8,598	8,598	25,337	883,607	4,159,681	2,662.4	1	1	8,199,181	6,513,152.6	1.05	102.77	2.95	34.87	3.76	3.76
2005	7,382	7,382	19,910	728,607	1,701,535	2,202.6	1	1	8,441,283	6,859,145.5	0.87	98.70	2.70	36.60	4.54	4.54
2006	16,391	16,391	49,955	1,874,070	4,150,900	5,602.7	2	2	19,125,858	11,508,952.8	0.86	114.34	3.05	37.52	3.57	3.57
2007	26,137	26,137	78,334	2,776,985	6,034,356	8,376.4	4	4	22,769,974	16,358,618.0	1.15	106.25	3.00	35.45	4.78	4.78
2008	45,282	45,282	120,803	4,056,250	8,718,620	12,426.4	3	3	43,364,885	26,924,515.0	1.04	89.58	2.67	33.58	2.41	2.41
2009	63,578	63,578	171,289	5,660,671	12,240,558	17,344.6	5	6	45,200,960	34,555,186.3	1.41	89.04	2.69	33.05	2.88	3.46
2010	61,843	61,843	162,103	5,352,517	11,616,799	16,427.4	8	10	43,372,749	33,305,663.7	1.43	86.55	2.62	33.02	4.87	6.09
2011	58,905	58,905	145,297	4,783,146	10,080,814	14,733.5	6	8	42,190,222	32,706,696.4	1.40	81.20	2.47	32.92	4.07	5.43
2012	65,577	65,577	146,131	4,686,640	9,595,450	14,575.3	8	8	41,050,084	31,518,525.9	1.60	71.47	2.23	32.07	5.49	5.49
2013	26,471	26,471	46,082	1,371,089	2,761,337	4,332.9	1	1	31,590,551	11,755,893.0	0.84	51.80	1.74	29.75	2.31	2.31
Primary diagnosis																
2000	549	549	1,814	64,137	192,109	190.8	0	0	7,045,322	3,216,544.6	0.08	116.83	3.30	35.36	0.00	0.00
2001	2,146	2,146	6,042	212,142	546,019	639.4	1	1	7,643,433	6,360,440.1	0.28	98.85	2.82	35.11	15.64	15.64
2002	3,775	3,775	12,064	469,199	1,121,523	1,391.0	0	0	7,768,829	6,427,334.6	0.49	124.29	3.20	38.89	0.00	0.00
2003	7,851	7,851	25,569	906,812	2,436,774	2,704.7	0	0	7,691,118	6,347,011.5	1.02	115.50	3.26	35.47	0.00	0.00
2004	8,598	8,598	25,337	883,607	4,159,681	2,662.4	1	1	8,199,181	6,513,152.6	1.05	102.77	2.95	34.87	3.76	3.76
2005	7,382	7,382	19,910	728,607	1,701,535	2,202.6	1	1	8,441,283	6,859,146.2	0.87	98.70	2.70	36.60	4.54	4.54
2006	16,391	16,391	49,955	1,874,070	4,150,900	5,602.7	1	1	19,125,859	11,508,957.8	0.86	114.34	3.05	37.52	1.78	1.78
2007	26,137	26,137	78,334	2,776,985	6,034,356	8,376.5	3	3	22,769,975	16,358,627.9	1.15	106.25	3.00	35.45	3.58	3.58
2008	45,283	45,283	120,804	4,056,280	8,718,680	12,427.7	2	2	43,364,888	26,924,558.1	1.04	89.58	2.67	33.58	1.61	1.61
2009	63,579	63,579	171,290	5,660,701	12,240,618	17,344.8	3	4	45,200,965	34,555,262.6	1.41	89.03	2.69	33.05	1.73	2.31
2010	61,845	61,845	162,105	5,352,577	11,616,889	16,427.8	5	7	43,372,750	33,305,729.5	1.43	86.55	2.62	33.02	3.04	4.26
2011	58,907	58,907	145,299	4,783,167	10,080,842	14,733.7	4	6	42,190,220	32,706,760.2	1.40	81.20	2.47	32.92	2.71	4.07
2012	65,581	65,581	146,137	4,686,814	9,595,951	14,576.2	7	7	41,050,083	31,518,591.8	1.60	71.47	2.23	32.07	4.80	4.80
2013	26,471	26,471	46,082	1,371,089	2,761,337	4,332.9	1	1	31,590,551	11,755,921.2	0.84	51.80	1.74	29.75	2.31	2.31

Table 4: Incident Drug Use (Incident to All Drugs in Appendix B) in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and May 31, 2013, by Drug Product, Event Washout Period, Primary Diagnosis Indicator, and Year

	New Users	New Episodes	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Number of Events	Eligible Members	Member-Years	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings /User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk	Total Number of Events / 10K Years at Risk	
183-day event washout																
Nonsecondary diagnosis																
2000	549	549	1,814	64,137	192,109	190.8	0	0	7,045,228	3,216,422.8	0.08	116.83	3.30	35.36	0.00	0.00
2001	2,145	2,145	6,031	211,812	545,089	638.5	1	1	7,643,360	6,360,211.8	0.28	98.75	2.81	35.12	15.66	15.66
2002	3,774	3,774	12,062	469,139	1,121,283	1,390.9	0	0	7,768,765	6,427,093.8	0.49	124.31	3.20	38.89	0.00	0.00
2003	7,851	7,851	25,569	906,812	2,436,774	2,704.7	0	0	7,691,057	6,346,806.7	1.02	115.50	3.26	35.47	0.00	0.00
2004	8,598	8,598	25,337	883,607	4,159,681	2,662.4	1	1	8,199,108	6,512,928.0	1.05	102.77	2.95	34.87	3.76	3.76
2005	7,381	7,381	19,909	728,585	1,701,498	2,202.5	1	1	8,441,216	6,858,911.6	0.87	98.71	2.70	36.60	4.54	4.54
2006	16,387	16,387	49,948	1,873,757	4,150,258	5,601.7	2	2	19,125,331	11,508,106.7	0.86	114.34	3.05	37.51	3.57	3.57
2007	26,135	26,135	78,332	2,776,940	6,034,311	8,376.2	4	4	22,769,320	16,357,180.5	1.15	106.25	3.00	35.45	4.78	4.78
2008	45,275	45,275	120,796	4,056,044	8,717,928	12,425.7	2	2	43,363,507	26,921,777.9	1.04	89.59	2.67	33.58	1.61	1.61
2009	63,566	63,566	171,239	5,659,224	12,237,516	17,340.4	4	4	45,199,690	34,551,528.9	1.41	89.03	2.69	33.05	2.31	2.31
2010	61,829	61,829	162,079	5,351,838	11,615,364	16,425.3	7	7	43,371,625	33,302,307.4	1.43	86.56	2.62	33.02	4.26	4.26
2011	58,896	58,896	145,276	4,782,535	10,079,497	14,731.6	6	8	42,189,073	32,703,330.8	1.40	81.20	2.47	32.92	4.07	5.43
2012	65,567	65,567	146,110	4,686,092	9,594,388	14,573.6	8	8	41,048,973	31,515,155.8	1.60	71.47	2.23	32.07	5.49	5.49
2013	26,466	26,466	46,075	1,370,872	2,760,970	4,332.2	1	1	31,589,006	11,754,615.9	0.84	51.80	1.74	29.75	2.31	2.31
Primary diagnosis																
2000	549	549	1,814	64,137	192,109	190.8	0	0	7,045,228	3,216,422.8	0.08	116.83	3.30	35.36	0.00	0.00
2001	2,145	2,145	6,031	211,812	545,089	638.5	1	1	7,643,360	6,360,212.2	0.28	98.75	2.81	35.12	15.66	15.66
2002	3,774	3,774	12,062	469,139	1,121,283	1,390.9	0	0	7,768,765	6,427,093.8	0.49	124.31	3.20	38.89	0.00	0.00
2003	7,851	7,851	25,569	906,812	2,436,774	2,704.7	0	0	7,691,057	6,346,806.7	1.02	115.50	3.26	35.47	0.00	0.00
2004	8,598	8,598	25,337	883,607	4,159,681	2,662.4	1	1	8,199,108	6,512,928.1	1.05	102.77	2.95	34.87	3.76	3.76
2005	7,381	7,381	19,909	728,585	1,701,498	2,202.5	1	1	8,441,220	6,858,925.8	0.87	98.71	2.70	36.60	4.54	4.54
2006	16,390	16,390	49,952	1,873,950	4,150,540	5,602.4	1	1	19,125,407	11,508,209.2	0.86	114.33	3.05	37.52	1.78	1.78
2007	26,135	26,135	78,332	2,776,940	6,034,311	8,376.3	3	3	22,769,363	16,357,364.1	1.15	106.25	3.00	35.45	3.58	3.58
2008	45,280	45,280	120,801	4,056,187	8,718,214	12,427.4	1	1	43,364,175	26,922,683.1	1.04	89.58	2.67	33.58	0.80	0.80
2009	63,573	63,573	171,248	5,659,470	12,238,042	17,341.3	2	2	45,200,256	34,553,086.5	1.41	89.02	2.69	33.05	1.15	1.15
2010	61,837	61,837	162,090	5,352,129	11,615,881	16,426.3	5	7	43,372,099	33,303,716.2	1.43	86.55	2.62	33.02	3.04	4.26
2011	58,903	58,903	145,290	4,782,916	10,080,455	14,732.9	4	6	42,189,481	32,704,599.6	1.40	81.20	2.47	32.92	2.72	4.07
2012	65,577	65,577	146,125	4,686,479	9,595,310	14,575.2	7	7	41,049,414	31,516,498.5	1.60	71.47	2.23	32.07	4.80	4.80
2013	26,467	26,467	46,076	1,370,902	2,761,030	4,332.3	1	1	31,589,608	11,755,169.5	0.84	51.80	1.74	29.75	2.31	2.31

Appendix A. Available Data in the Mini-Sentinel Distributed Database (MSDD) for Each Data Partner (DP) as of Request Send Date (April 11, 2014)

DP ID	Start Date	End Date
DP001	1/1/2000	5/31/2013
DP002	1/1/2000	5/31/2013
DP003	1/1/2000	5/31/2013
DP004	1/1/2000	5/31/2013
DP005	1/1/2000	5/31/2013
DP006	1/1/2000	5/31/2013
DP007	1/1/2000	5/31/2013
DP008	1/1/2000	5/31/2013
DP009	1/1/2000	5/31/2013
DP010	1/1/2000	5/31/2013
DP011	1/1/2000	5/31/2013
DP012	1/1/2000	5/31/2013
DP013	1/1/2000	5/31/2013
DP014	1/1/2000	5/31/2013
DP015	1/1/2000	5/31/2013

Appendix B: Generic and Brand Names Used to Define Exposures in this Report

Generic Name	Brand Name
CARBAMAZEPINE	CARBAMAZEPINE
CARBAMAZEPINE	EQUETRO
CARBAMAZEPINE	CARBATROL
CARBAMAZEPINE	TEGRETOL
CARBAMAZEPINE	EPITOL
CARBAMAZEPINE	ATRETOL
CARBAMAZEPINE	TEGRETOL XR
CARBAMAZEPINE	CARBAMAZEPINE XR
CARBAMAZEPINE	CARBAMAZEPINE ER
LAMOTRIGINE	LAMOTRIGINE
LAMOTRIGINE	LAMICTAL
LAMOTRIGINE	LAMICTAL (GREEN)
LAMOTRIGINE	LAMICTAL (ORANGE)
LAMOTRIGINE	LAMICTAL (BLUE)
LAMOTRIGINE	LAMICTAL XR
LAMOTRIGINE	LAMICTAL XR (BLUE)
LAMOTRIGINE	LAMICTAL XR (GREEN)
LAMOTRIGINE	LAMICTAL XR (ORANGE)
LAMOTRIGINE	LAMICTAL ODT
LAMOTRIGINE	LAMICTAL ODT (ORANGE)
LAMOTRIGINE	LAMICTAL ODT (BLUE)
LAMOTRIGINE	LAMICTAL ODT (GREEN)
LEVETIRACETAM	LEVETIRACETAM
LEVETIRACETAM	KEPPRA
LEVETIRACETAM	KEPPRA XR
TOPIRAMATE	TOPAMAX
TOPIRAMATE	TOPIRAMATE
TOPIRAMATE	TOPIRAGEN
TOPIRAMATE	TROKENDI XR
CLOZAPINE	CLOZARIL
CLOZAPINE	CLOZAPINE
CLOZAPINE	CLOZAPINE ODT
CLOZAPINE	FAZACLO
CLOZAPINE	VERSACLOZ
OLANZAPINE/FLUOXETINE HCL	SYMBYAX
OLANZAPINE/FLUOXETINE HCL	OLANZAPINE-FLUOXETINE HCL
OLANZAPINE	ZYPREXA
OLANZAPINE	ZYPREXA ZYDIS
OLANZAPINE	OLANZAPINE
OLANZAPINE	OLANZAPINE ODT

Appendix C: International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis Codes Used to Define Agranulocytosis Events in this Report

Code*	Description
288	Diseases of white blood cells
288.0	Neutropenia
288.00	Neutropenia, unspecified
288.01	Congenital neutropenia
288.02	Cyclic neutropenia
288.03	Drug induced neutropenia
288.04	Neutropenia due to infection
288.09	Other neutropenia
288.2	Genetic anomalies of leukocytes
288.4	Hemophagocytic syndromes
288.5	Decreased white blood cell count
288.50	Leukocytopenia, unspecified
288.59	Other decreased white blood cell count
288.9	Unspecified disease of white blood cells

* exact match query

Appendix D. Specifications for Query ID to09y05_mpr_wp26_v01

Modular Program #3 was used to investigate diagnosis of agranulocytosis following new use of several anti-epileptic drugs (AEDs), as well as clozapine and olanzapine. Five runs of the program were required. In total, forty different scenarios were examined in this request with differing exposures of interest, incidence criteria, event washout period, and event care setting. See below for a description of each of these scenarios. Report 2 presents scenarios 25-40 where the exposures are incident to a list of other drugs (Appendix B) in addition to the drug of interest.

Coverage Requirement	Drug and Medical Coverage
Query Period	January 1, 2000 to May 31, 2013
Enrollment Gap	45 Days
Minimum Enrollment Days	183 Days
Age Stratifications	<18, 18-<45, 45-<65, 65+ Years

Scenario	Drug/Exposure									Event/Outcome			
	Incident exposure	Incident w/ respect to:	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Minimum Days Supplied	Minimum Episode Duration	Episode Truncation by Incident Exposure	Event/ Outcome	Washout Period	Event De-duplication	Care Setting/ PDX
1	Carbamazepine	Carbamazepine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IP non-secondary
2	Levetiracetam	Levetiracetam	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IP non-secondary
3	Lamotrigine	Lamotrigine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IP non-secondary
4	Topiramate	Topiramate	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IP non-secondary
5	Clozapine	Clozapine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IP non-secondary
6	Olanzapine	Olanzapine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IP non-secondary
7	Carbamazepine	Carbamazepine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IPP
8	Levetiracetam	Levetiracetam	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IPP
9	Lamotrigine	Lamotrigine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IPP
10	Topiramate	Topiramate	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IPP
11	Clozapine	Clozapine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IPP
12	Olanzapine	Olanzapine	183	01 (SING)	10	10	1	1	No	agranulocytosis	7	2	IPP
13	Carbamazepine	Carbamazepine	183	01 (SING)	10	10	1	1	No	agranulocytosis	183	2	IP non-secondary
14	Levetiracetam	Levetiracetam	183	01 (SING)	10	10	1	1	No	agranulocytosis	183	2	IP non-secondary

15	<i>Lamotrigine</i>	<i>Lamotrigine</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IP non-secondary
16	<i>Topiramate</i>	<i>Topiramate</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IP non-secondary
17	<i>Clozapine</i>	<i>Clozapine</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IP non-secondary
18	<i>Olanzapine</i>	<i>Olanzapine</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IP non-secondary
19	<i>Carbamazepine</i>	<i>Carbamazepine</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IPP
20	<i>Levetiracetam</i>	<i>Levetiracetam</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IPP
21	<i>Lamotrigine</i>	<i>Lamotrigine</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IPP
22	<i>Topiramate</i>	<i>Topiramate</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IPP
23	<i>Clozapine</i>	<i>Clozapine</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IPP
24	<i>Olanzapine</i>	<i>Olanzapine</i>	183	<i>01 (SING)</i>	10	10	1	1	No	agranulocytosis	183	2	IPP
25	Carbamazepine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IP non-secondary
26	Lamotrigine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IP non-secondary
27	Levetiracetam	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IP non-secondary
28	Topiramate	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IP non-secondary
29	Carbamazepine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IPP
30	Lamotrigine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IPP
31	Levetiracetam	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IPP
32	Topiramate	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	7	2	IPP
33	Carbamazepine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IP non-secondary
34	Lamotrigine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IP non-secondary
35	Levetiracetam	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IP non-secondary
36	Topiramate	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IP non-secondary
37	Carbamazepine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IPP
38	Lamotrigine	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IPP
39	Levetiracetam	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IPP
40	Topiramate	All Oral AEDs	183	01 (SING)	10	10	1	1	YES	agranulocytosis	183	2	IPP

Scenarios 1-24 (in italics) are presented in Report 1