Disclaimer

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

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

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

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

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Overview for Request cder_mpl1r_wp059

Request ID: cder_mpl1r_wp059_nsdp_v01

Report Description: The goal of this report was to characterize the uptake and utilization of Qsymia (combination product of phentermine and topiramate), phentermine, and topiramate in the Sentinel Distributed Database (SDD). This report includes the distribution of days supply, length of treatment episodes, and time to initiation. This is report 1 of 2. The second report estimates the number of incident users of these drugs along with concomitant phentermine and topiramate, with additional estimates among individuals with a history of either epilepsy or seizures, with a history of migraines, and with no history of those conditions.

Sentinel Modular Program Tool Used: Modular Program 8, version 2.6

Data Source: Data from September 17, 2012 to April 30, 2017 from 16 Data Partners contributing to the SDD were included in this report. This request was distributed on August 17, 2017. See Appendix A for a list of the dates of available data for each Data Partner.

Exposures of Interest: There were three exposures of interest in this request: Qsymia, phentermine, and topiramate. Please see Appendix B for generic and brand names used to define the exposures of interest.

Cohort Eligibility Criteria: Individuals were required to be continuously enrolled in health plans with both medical and drug coverage for at least 183 days prior to their first qualifying dispensing date, during which gaps in coverage of up to 30 days were allowed. Individuals were excluded if they had evidence of Qsymia, phentermine, or topiramate in the 183 days prior to the first qualifying dispensing date of the exposure of interest. The following age groups were included: 18-44, 45-64, and 65+ years. All qualifying incident dispensings that occurred between September 17, 2012 and April 30, 2017 were included, and a gap of 30 days was allowed between dispensings to be considered part of the same episode. The end date of each exposure episode was extended by 30 additional days.

Limitations: Algorithms to define exposures and baseline characteristics are imperfect and may be misclassified. Therefore, data should be interpreted with this limitation in mind.

Please see the Appendix C for the specifications of parameters to be used in the analyses for this request.

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

Sentinel

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

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

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

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

- **Ambulatory Visit (AV) -** includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.
- **Emergency Department (ED) -** includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.
- **Inpatient Hospital Stay (IP) -** includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.
- **Non-Acute Institutional Stay (IS) -** includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.
- **Other Ambulatory Visit (OA) -** includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

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

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

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

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a “continuously enrolled”

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

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

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

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

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

Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition

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

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

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

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

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

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

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

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

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

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

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

*all terms may not be used in this report

Table 1. Descriptive Statistics for Number of Days Supplied per Dispensing in the Sentinel Distributed Database (SDD) from September 17, 2012 to August 15, 2017

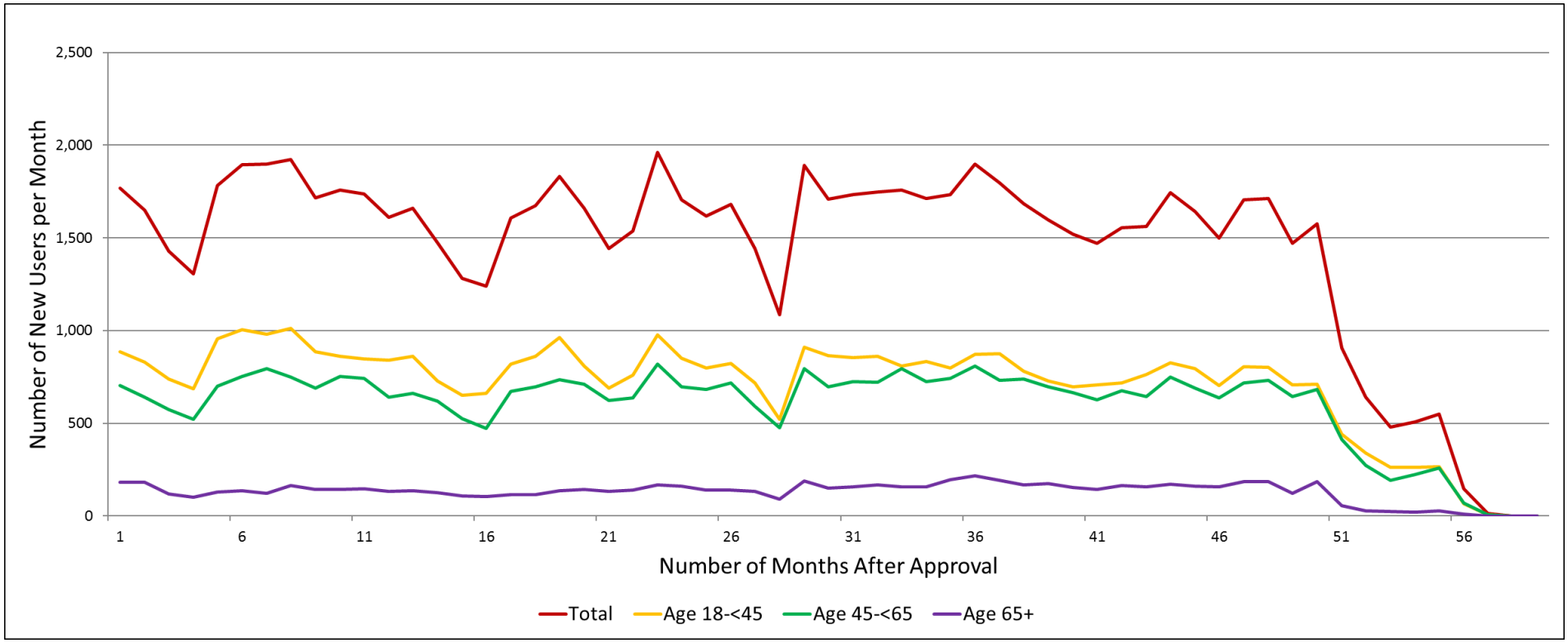
	Phentermine	Qsymia	Topiramate
Total Dispensings	303,358	32,553	1,916,732
Minimum	1	1	1
1st Percentile	7	14	15
5th Percentile	30	14	30
25th Percentile	30	30	30
Mean	32.4	29.4	36.1
Median	30	30	30
Mode	30	30	30
75th Percentile	30	30	30
95th Percentile	60	30	90
99th Percentile	90	44	100
Maximum	999	234	999

Table 2. Descriptive Statistics for Length (in Days) of Treatment Episodes* by Drug in the Sentinel Distributed Database (SDD) from September 17, 2012 to August 15, 2017

	Number of Patients (%)	Median	Mean	Standard Deviation
Phentermine				
Episode 1	85,333 (100.00%)	76	107.79	319.81
Episode 2	29,889 (35.03%)	60	94.2	211.84
Episode 3	12,641 (14.81%)	60	91.03	164.01
Episode 4	5,886 (6.90%)	60	86.86	128.97
Episode 5	2,866 (3.36%)	60	84.01	99.87
Episode 6	1,437 (1.68%)	60	81.23	93.8
Qsymia				
Episode 1	7,495 (100.00%)	90	134.53	239.28
Episode 2	1,699 (22.67%)	60	112.09	160.28
Episode 3	551 (7.35%)	60	111.48	154.8
Episode 4	191 (2.55%)	60	95.3	100.37
Episode 5	70 (0.93%)	60	89.01	77.88
Episode 6	25 (0.33%)	60	71.76	67.84
Topiramate				
Episode 1	413,015 (100.00%)	75	148.91	852.75
Episode 2	105,840 (25.63%)	72	134.27	484.23
Episode 3	41,975 (10.16%)	67	124.81	335.96
Episode 4	19,430 (4.70%)	60	115.85	253.59
Episode 5	9,684 (2.34%)	60	110.76	204.94
Episode 6	4,876 (1.18%)	60	102.3	166.22

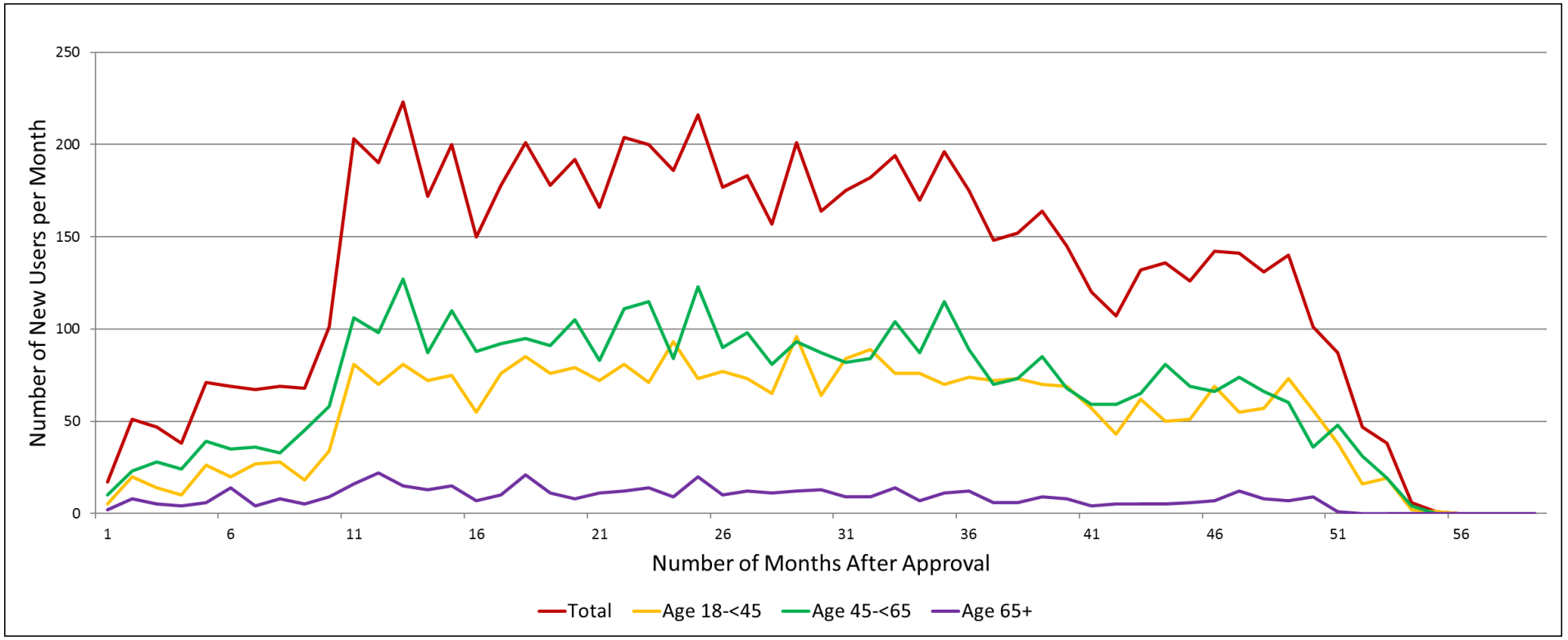
*This request only included individuals' first six episodes; however, individuals included in this request may have had more than six episodes.

Figure 1a. New Users of Phentermine and Number of Months Dispensed After Qsymia Approval[1] by Age Group



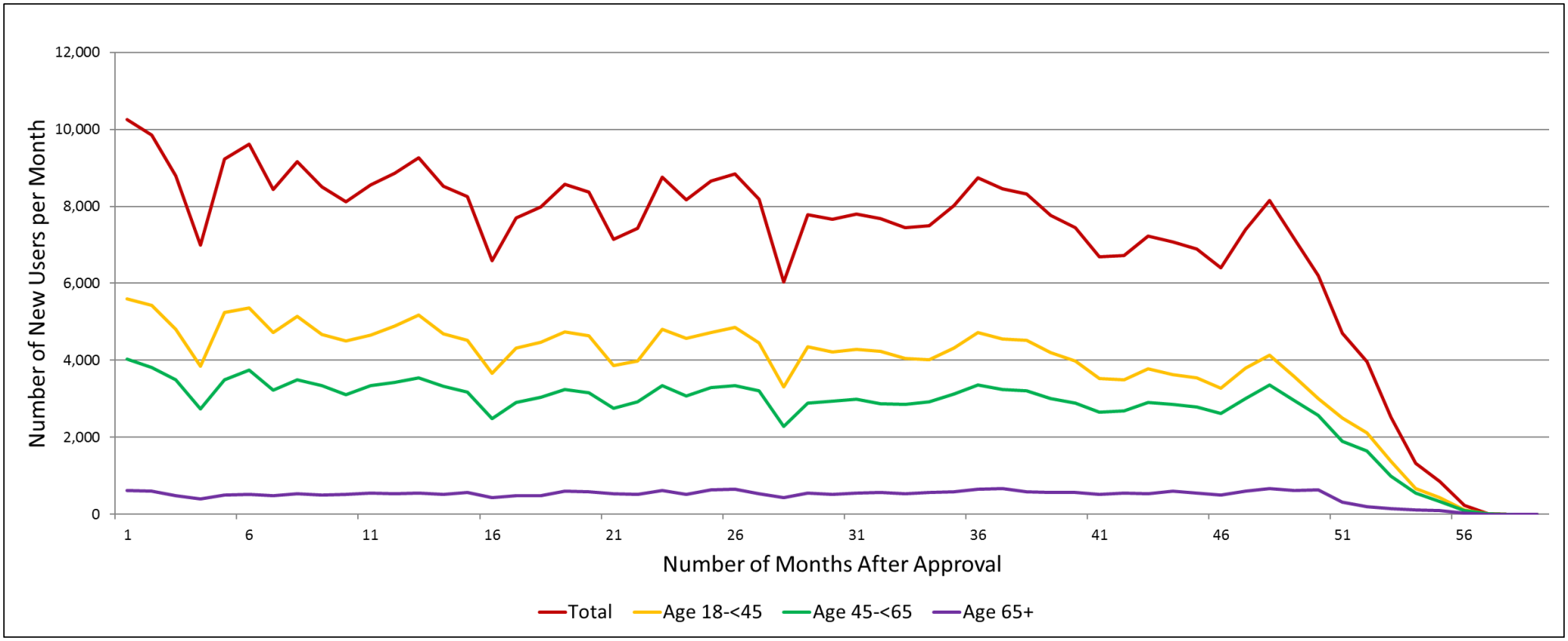
[1]Qsymia approval date: September 17, 2012

Figure 1b. New Users of Qsymia and Number of Months Dispensed After Qsymia Approval[1] by Age Group



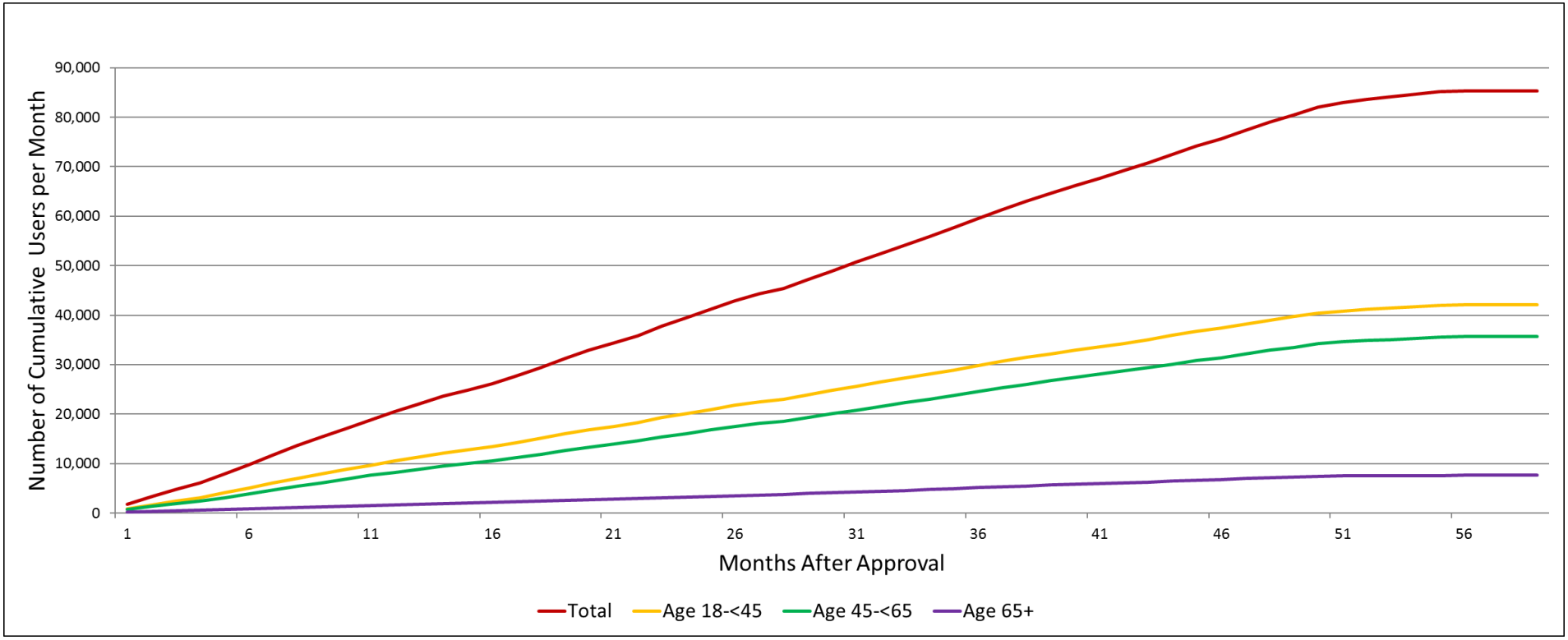
[1]Qsymia approval date: September 17, 2012.

Figure 1c. New Users of Topiramate and Number of Months Dispensed After Qsymia Approval[1] by Age Group



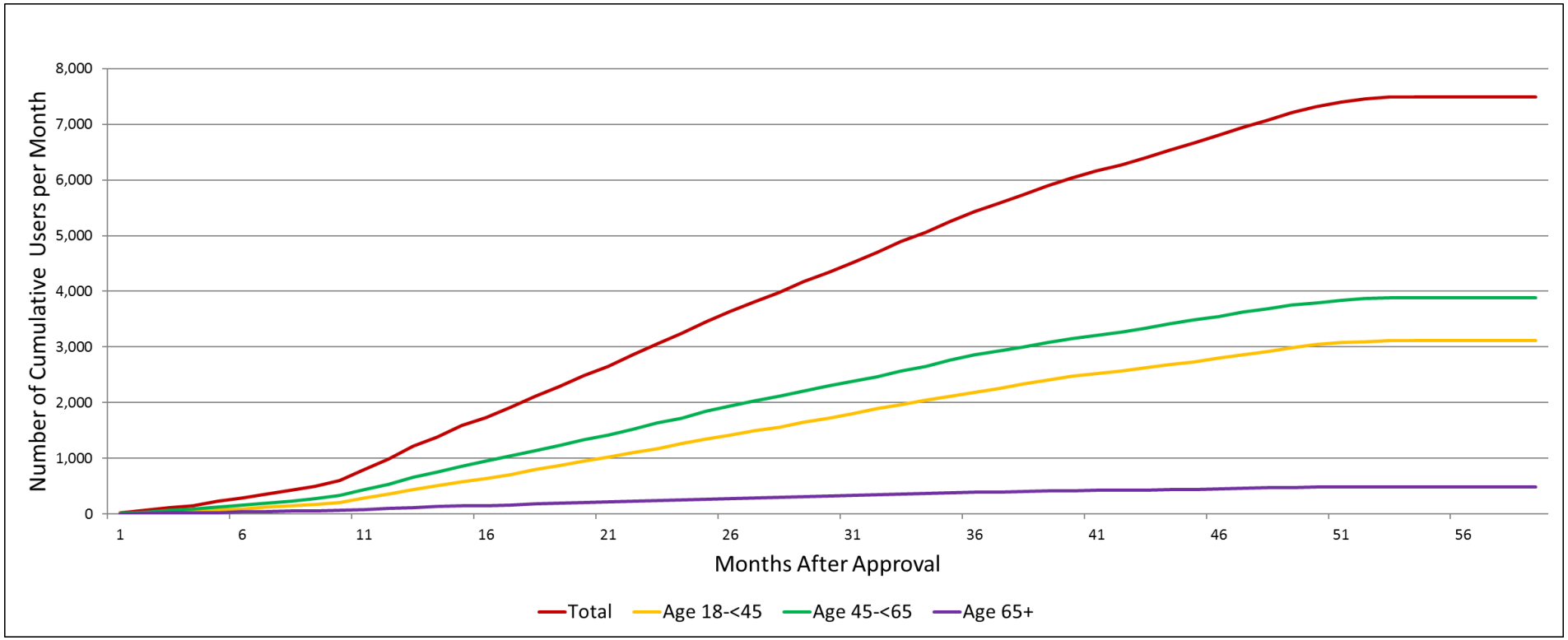
[1]Qsymia approval date: September 17, 2012.

Figure 2a. Cumulative Phentermine Users and Number of Months After Qsymia Approval[1] by Age Group



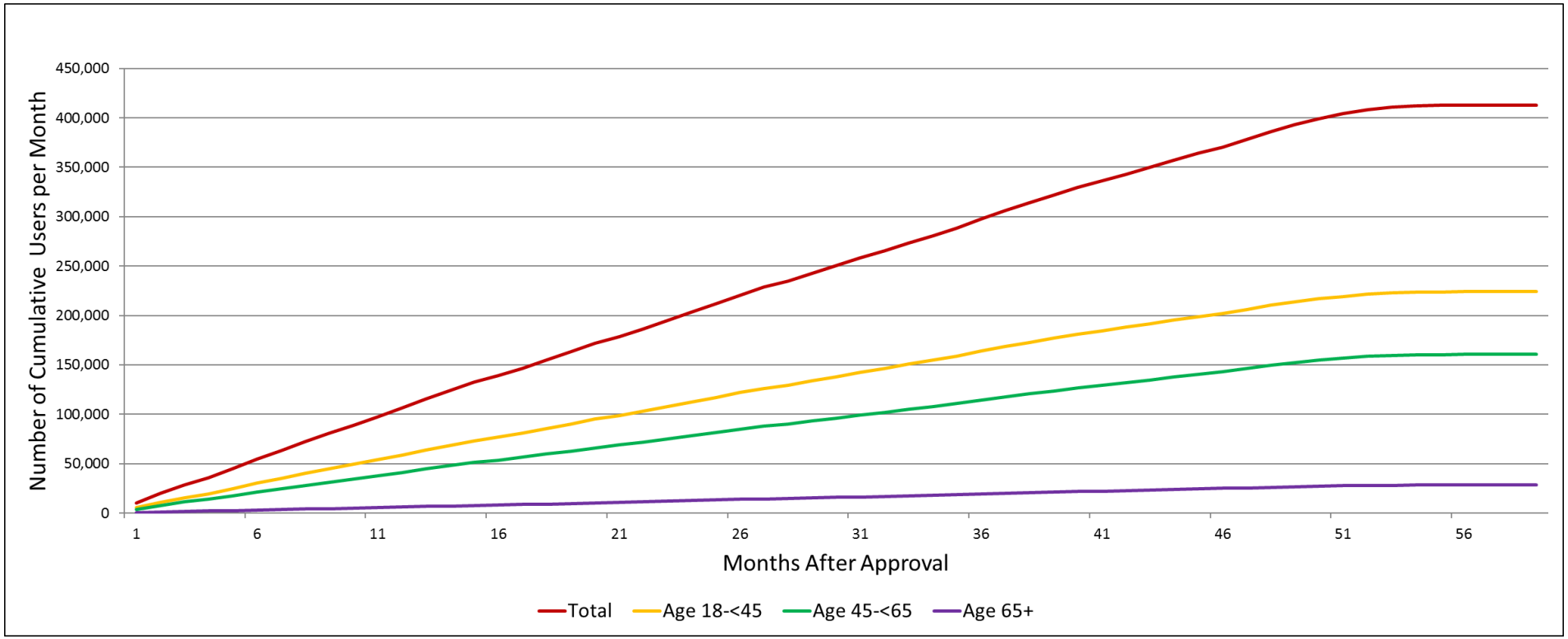
[1]Qsymia approval date: September 17, 2012.

Figure 2b. Cumulative Qsymia Users and Number of Months After Qsymia Approval[1] by Age Group



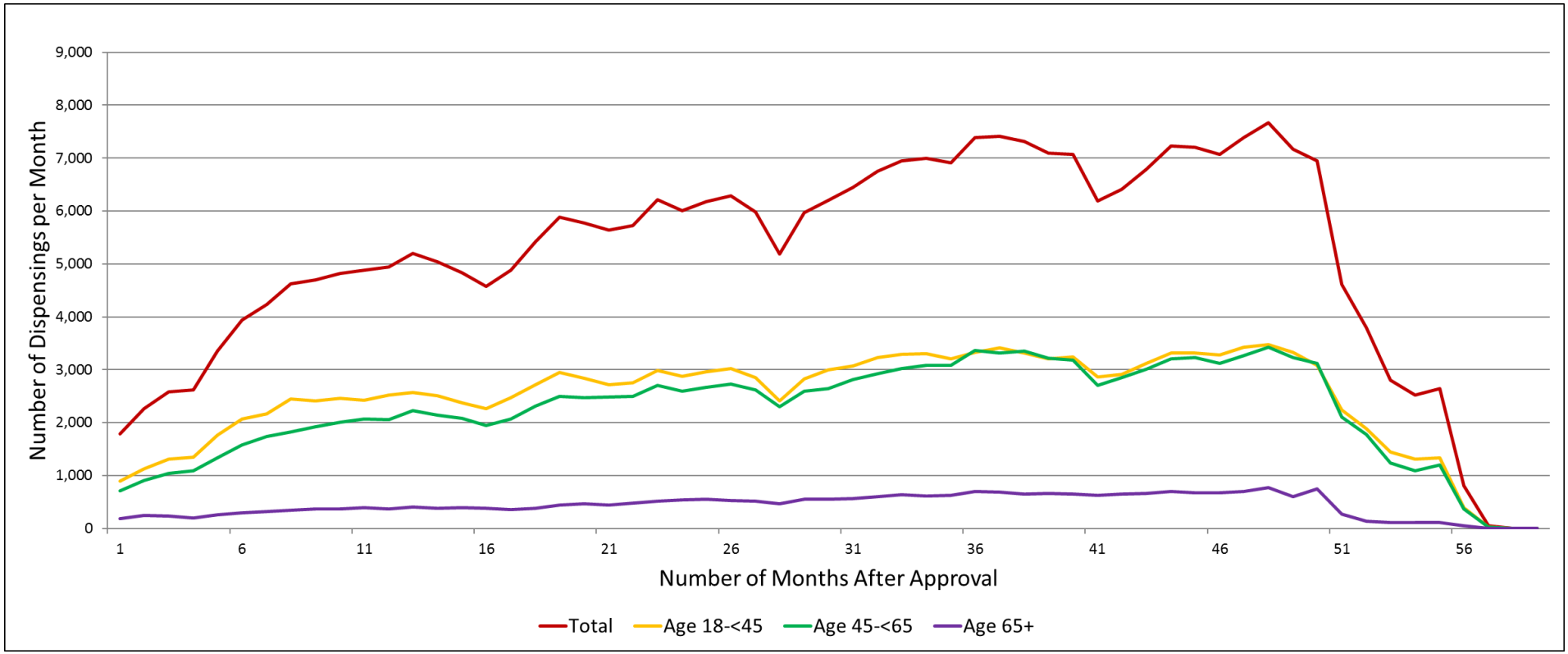
[1]Qsymia approval date: September 17, 2012.

Figure 2c. Cumulative Topiramate Users and Number of Months After Qsymia Approval[1] by Age Group



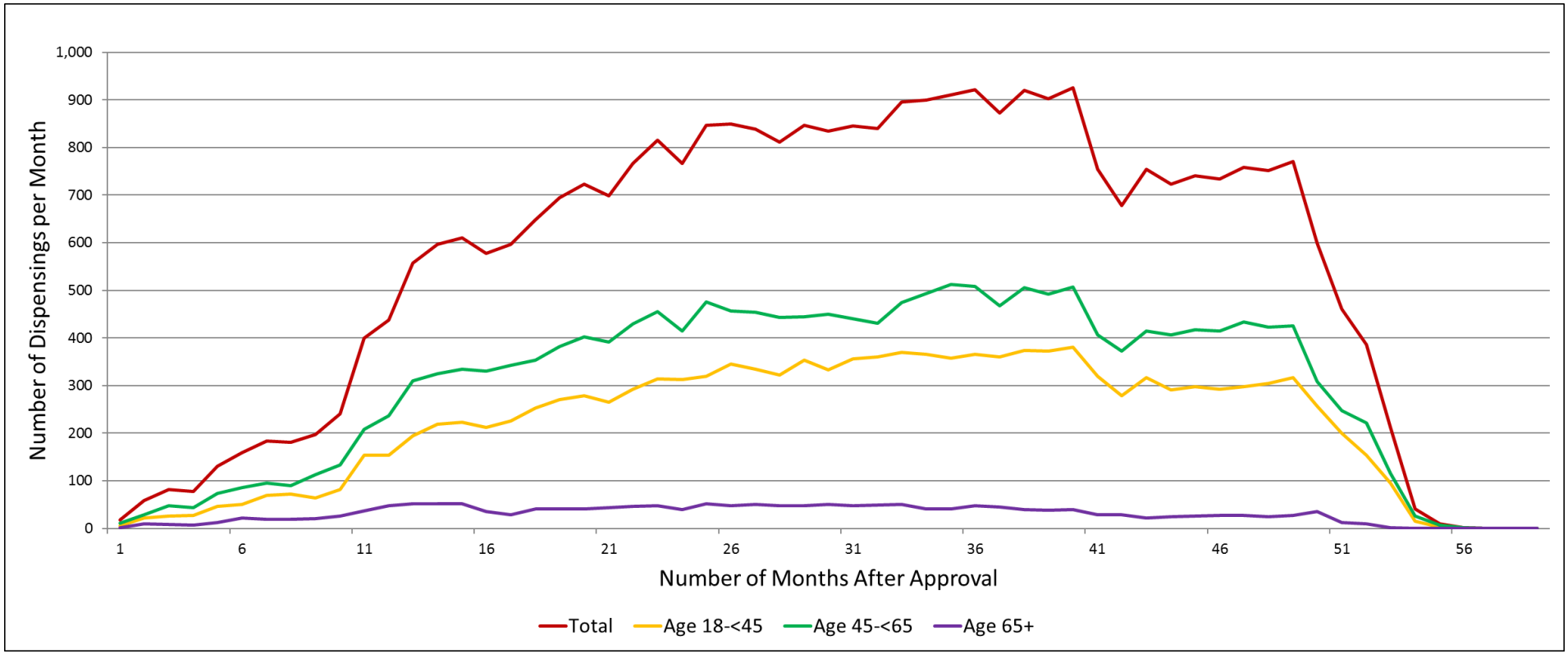
[1]Qsymia approval date: September 17, 2012.

Figure 3a. Phentermine Dispensings and Number of Months After Qsymia Approval[1] by Age Group



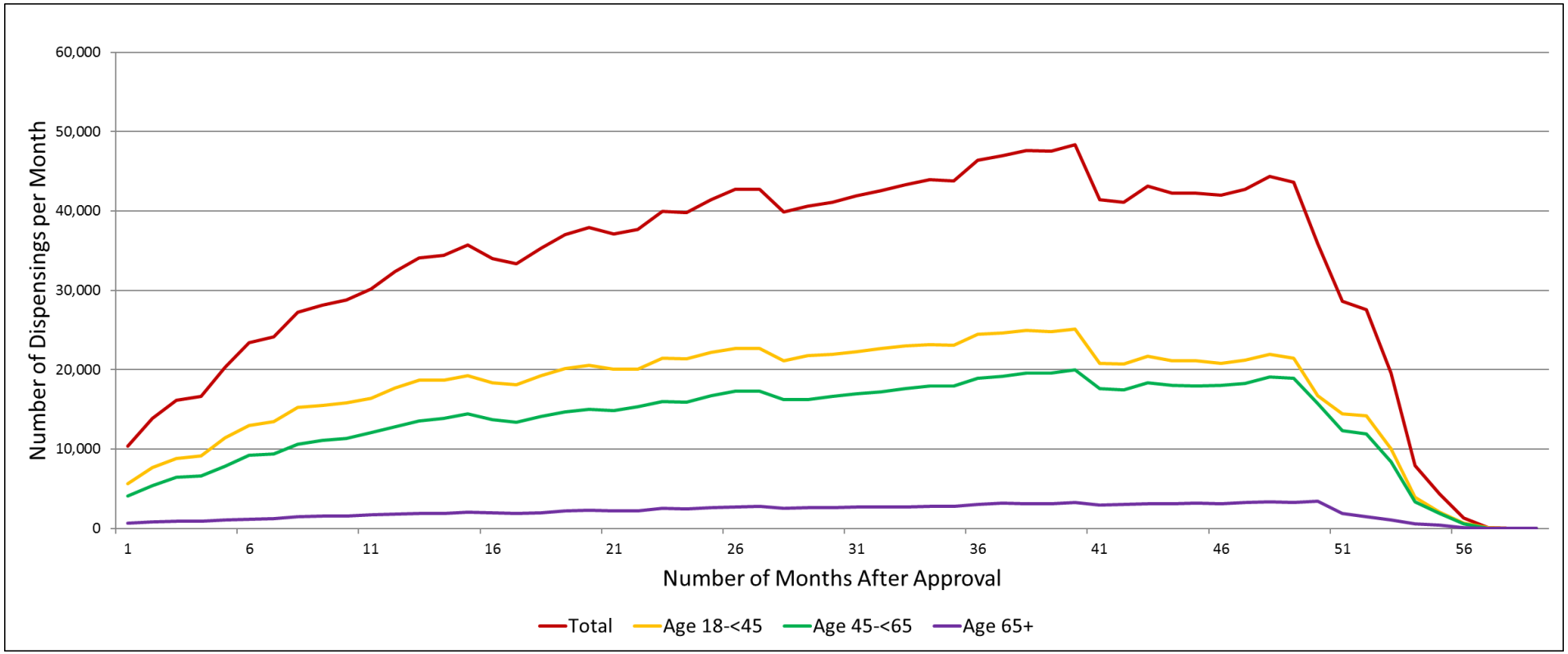
[1]Qsymia approval date: September 17, 2012.

Figure 3b. Qsymia Dispensings and Number of Months After Qsymia Approval[1] by Age Group



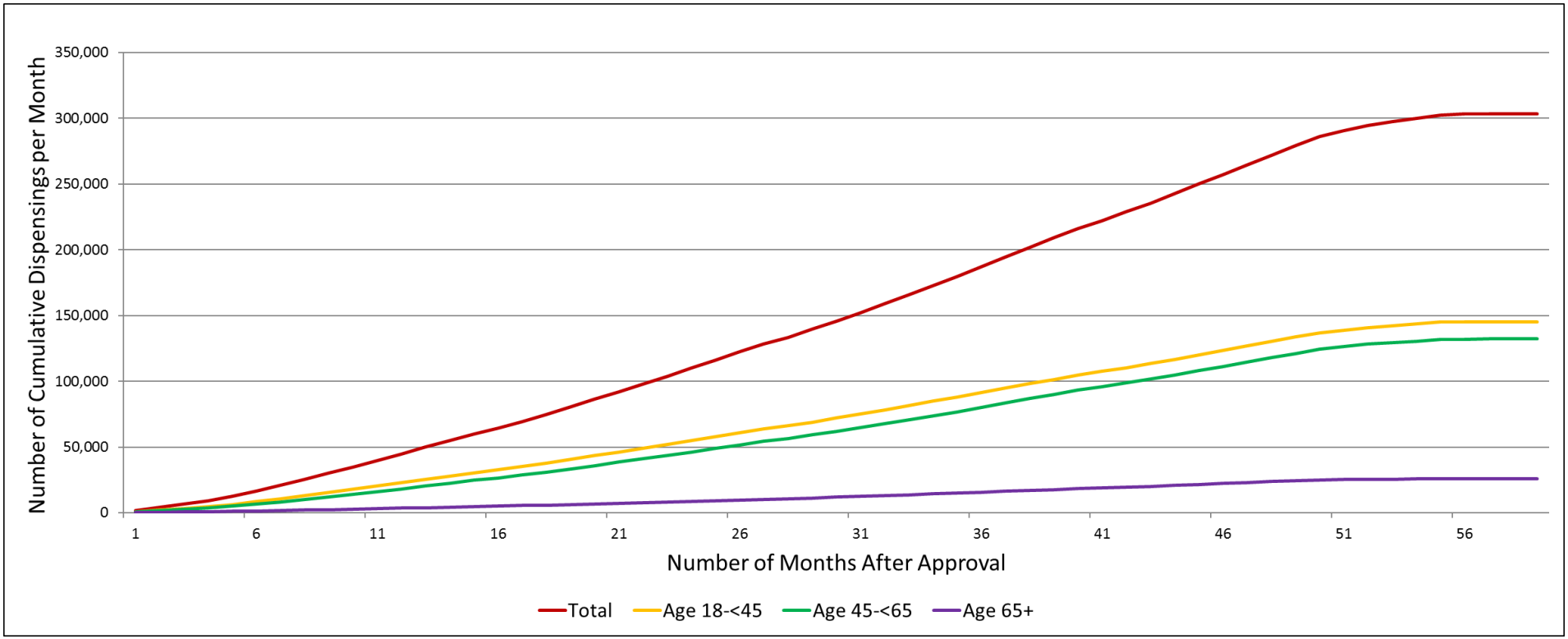
[1]Qsymia approval date: September 17, 2012.

Figure 3c. Topiramate Dispensings and Number of Months After Qsymia Approval[1] by Age Group



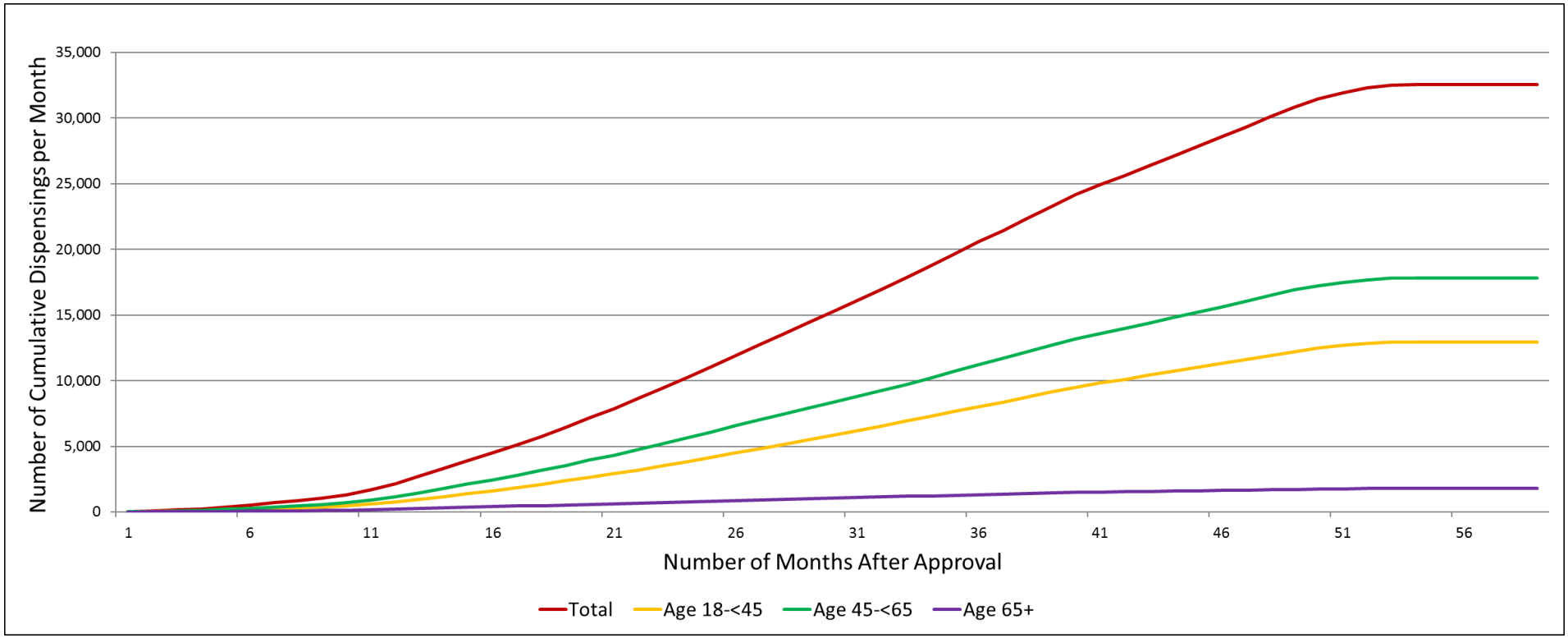
[1]Qsymia approval date: September 17, 2012.

Figure 4a. Phentermine Cumulative Number of Dispensings and Number of Months After Qsymia Approval[1] by Age Group



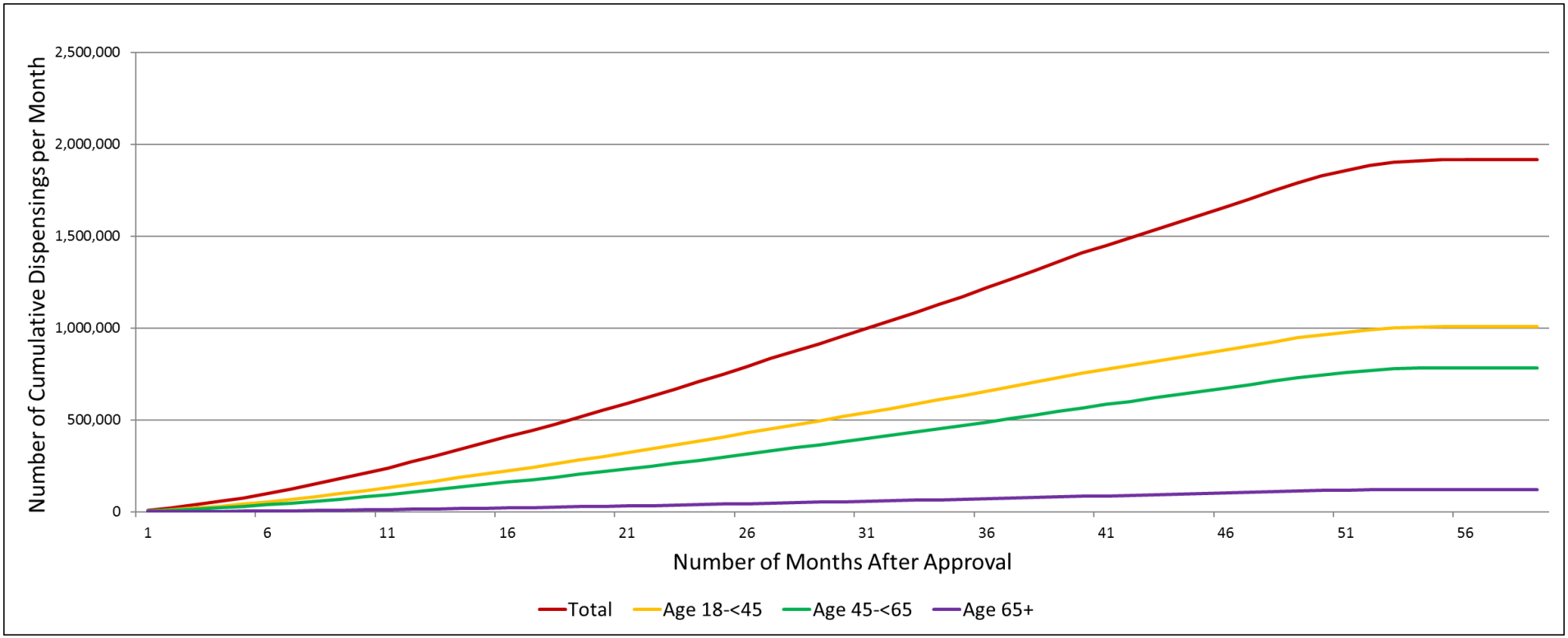
[1]Qsymia approval date: September 17, 2012.

Figure 4b. Qsymia Cumulative Number of Dispensings and Number of Months After Qsymia Approval[1] by Age Group



[1]Qsymia approval date: September 17, 2012.

Figure 4c. Topiramate Cumulative Number of Dispensings and Number of Months After Qsymia Approval[1] by Age Group



[1]Qsymia approval date: September 17, 2012.

Figure 5a. Distribution of New Users of Phentermine and Total Days Supplied

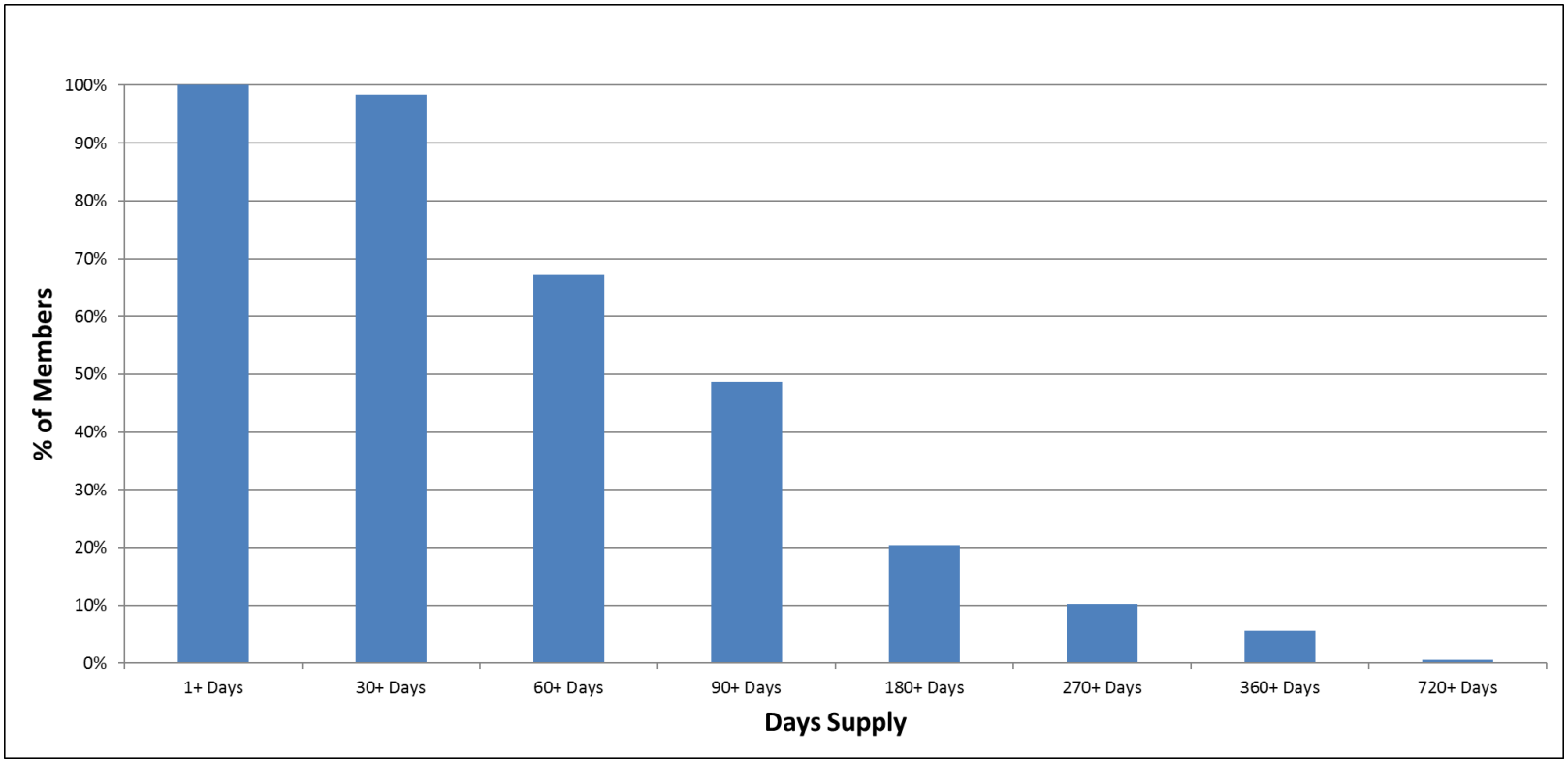


Figure 5b. Distribution of New Users of Qsymia and Total Days Supplied

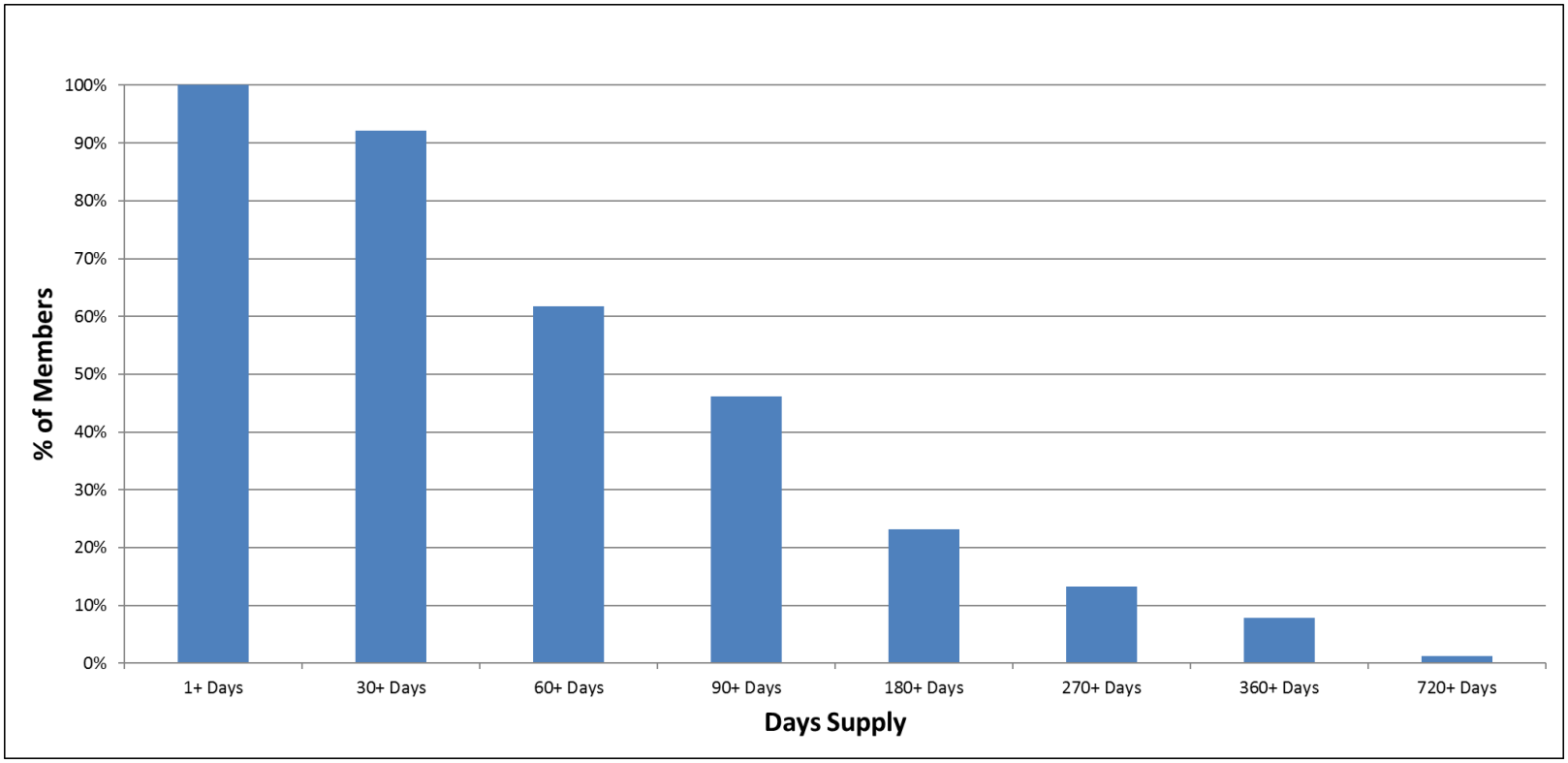
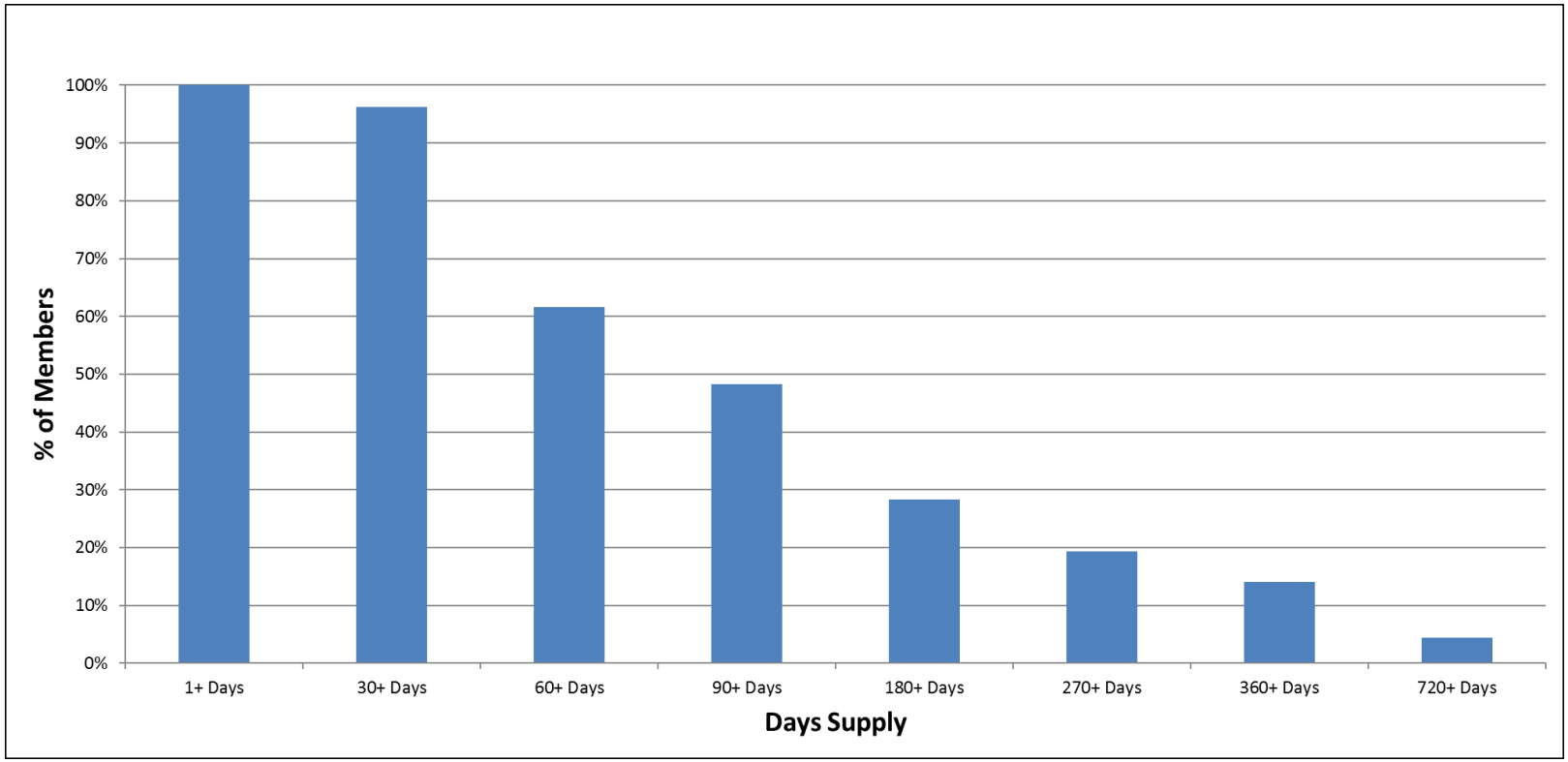


Figure 5c. Distribution of New Users of Topiramate and Total Days Supplied



Appendix A. List of Dates of Available Data for Each Data Partner (DP) in the Sentinel Distributed Database as of Request Distribution Date (August 17, 2017)

DP ID	Start Date[1]	End Date[1]
DP0001	9/17/2012	10/31/2014
DP0002	9/17/2012	5/31/2015
DP0003	9/17/2012	10/31/2015
DP0004	9/17/2012	12/31/2015
DP0005	9/17/2012	3/31/2016
DP0006	9/17/2012	6/30/2016
DP0007	9/17/2012	9/30/2016
DP0008	9/17/2012	10/31/2016
DP0009	9/17/2012	11/30/2016
DP0010	9/17/2012	1/31/2017
DP0011	9/17/2012	3/31/2017
DP0012	9/17/2012	3/31/2017
DP0013	9/17/2012	3/31/2017
DP0014	9/17/2012	3/31/2017
DP0015	9/17/2012	3/31/2017
DP0016	9/17/2012	4/30/2017

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

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

Generic Name	Brand Name
Qsymia	
PHENTERMINE HCL/TOPIRAMATE	Qsymia
Phentermine	
PHENTERMINE HCL	Phentermine
PHENTERMINE HCL	Adipex-P
PHENTERMINE HCL	Suprenza
PHENTERMINE HCL	Lomaira
Topiramate	
TOPIRAMATE	Topiramate
TOPIRAMATE	Topamax
TOPIRAMATE	Trokendi XR
TOPIRAMATE	Qudexy XR
TOPIRAMATE	Topiragen

Appendix C. Specifications for Request: cder_mpl1r_wp059_nsdp_v01

Modular Program #8 was used to characterize the uptake and utilization of Qsymia, phentermine, and topiramate.

Query Period: September 17, 2012 - August 15, 2017
Coverage Requirement: Medical and Drug
Enrollment Requirement: 183 days
Enrollment Gap: 30 days
Age Stratifications: 18-44, 45-64, 65+ years
Days of Supply Groups: 0-30, 31-60, 61-90, 91+ days
Total Days of Supply Thresholds: 001, 030, 060, 090, 180, 270, 360, 720 days

Scenario	Exposure	Washout Period (days)	Minimum Days Supplied	Maximum Days Supplied	Episode Gap	Exposure Extension Period	Minimum Episode Duration	Stockpiling Type
1	Qsymia	183	1	999	30	30	1	Standard*
2	Phentermine	183	1	999	30	30	1	Standard
3	Topiramate	183	1	999	30	30	1	Standard