



NDA 022580/S-032

**SUPPLEMENT APPROVAL**

VIVUS, LLC  
Attention: Maryam Azizi  
Senior Director, Global Regulatory Affairs  
900 East Hamilton Avenue  
Suite 550  
Campbell, CA 95008

Dear Maryam Azizi:

Please refer to your supplemental new drug application (sNDA) dated and received April 2, 2026, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Qsymia (phentermine and topiramate extended-release capsules).

This “Changes Being Effected” sNDA provides for proposed modifications to the approved Qsymia risk evaluation and mitigation strategy (REMS).

We have completed our review of this supplemental application, as amended. It is approved effective on the date of this letter.

**RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS**

The REMS for Qsymia was originally approved on July 17, 2012, and the most recent REMS modification was approved on July 11, 2025. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consists of modifications to the REMS to align the Qsymia REMS with S-031, approved on March 6, 2026, to include:

- Updating the Medication Guide to the approved version from S-031.
- Removing the “Important Safety Information” section from the Qsymia REMS Pharmacy Training and REMS Program Website.
- Global changes to the REMS materials including updated version codes and dates.

Your proposed modified REMS, submitted on April 2, 2026, amended and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on July 17, 2012.

The revised REMS assessment plan must include, but is not limited to, the following:

For each metric, provide the two previous, current, and cumulative reporting periods (if applicable or relevant) unless otherwise noted.

## **Implementation and Operations**

### **1. REMS Certification and Enrollment Statistics**

- a. Pharmacies
  - i. Number of certified pharmacies stratified by pharmacy type (i.e., mail order, chain, independent)
  - ii. Number and percentage of newly certified pharmacies stratified by pharmacy type (i.e., mail order, chain, independent)
  - iii. Number and percentage of active certified pharmacies (i.e., have dispensed Qsymia within the reporting period) stratified by pharmacy type (i.e., mail order, chain, independent)
- b. Distributors
  - i. Number of authorized distributors
  - ii. Number and percentage of newly authorized distributors
  - iii. Number and percentage of active authorized distributors (i.e., have shipped Qsymia within the reporting period)

### **2. REMS Utilization Data**

- a. Patient Demographics
  - i. Unique number of all patients who received Qsymia stratified by gender
  - ii. Unique number of patients of reproductive potential receiving Qsymia grouped by the following age ranges (years)
    - 1) 12 - <18
    - 2) 18 - <25
    - 3) 25 - <45
    - 4) 45 - <53
    - 5) 53+
  - iii. Average duration of Qsymia treatment among patients of reproductive potential based on patient age outlined above
- b. Prescription Data
  - i. A table that includes the following for the overall population and another table for patients of reproductive potential based on patient age as outlined above:
    - 1) Total number of unique patients
    - 2) Number and percentage of total prescriptions dispensed
    - 3) Number and percentage of total prescriptions dispensed for new prescriptions and refills
    - 4) Number and percentage of total prescriptions dispensed by dosage strength

### 3. REMS Compliance

#### a. Audits

- i. A report of audit findings for each stakeholder including but not limited to:
  - 1) A copy of the audit plan for each stakeholder
  - 2) Number of audits expected and performed
  - 3) Number and type of deficiencies (e.g., critical, major, or minor findings) noted for audited stakeholders
  - 4) Report of the number of those with deficiencies noted that successfully completed a corrective and preventative action plan (CAPA) within the timeframe specified in the audit plan
  - 5) Actions taken for those that did not complete the CAPA within the timeframe specified in the audit plan
  - 6) Unique identifiers for stakeholders that had deviations to track deviations by stakeholders over time
  - 7) Documentation of completion of training for relevant staff
  - 8) Verification of the existence of documented processes and procedures for complying with the REMS
  - 9) Comparison of the findings to findings of previous audits and an assessment of whether any trends are observed

#### b. Non-compliance

- i. A summary of the non-compliance identified, including but not limited to:
  - 1) A copy of the non-compliance plan which addresses the criteria for non-compliance for each stakeholder, actions taken to address non-compliance for each event, and under what circumstances a stakeholder would be suspended or decertified from the REMS
  - 2) Summary of non-compliance events identified per pharmacy and distributors including any CAPAs and status of corrective actions
  - 3) Number of instances of non-compliance accompanied by a description of each instance and the reason for the occurrence (if provided); for each instance of non-compliance report the following:
    - a) Unique identifier of the stakeholder(s) associated with the non-compliance event or deviation to enable tracking over time
    - b) Source of non-compliance data
    - c) Results of the root cause analysis
    - d) Actions taken in response and whether follow-up is planned
  - 4) Number and type of pharmacy decertified and the reason for decertification
  - 5) Summary of annual compliance reports provided to VIVUS by corporate chain entities, mail order pharmacies, and contracted

distributors

- c. Report on the periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24 and Risk of Birth Defects with Qsymia patient brochure
  - i. Pharmacist Materials Distribution Survey
    - 1) Assessment of pharmacists' compliance with the Qsymia REMS dispensing requirements, specifically the provision of a Medication Guide and Risk of Birth Defects with Qsymia patient brochure with each dispensing of Qsymia

## **Health Outcomes and/or Surrogates of Health Outcomes**

### **4. Safety Surveillance**

- a. Summary of pregnancy cases associated with Qsymia, including the following:
  - i. Event identification number
  - ii. Source of the report
  - iii. Contraceptive methods used
  - iv. Pregnancy outcome
  - v. Age of patient
  - vi. Cases of congenital malformations for each exposed pregnancy
- b. Follow-up of outstanding pregnancy reports from the previous assessment reporting period
- c. Root cause analysis of each reported pregnancy to determine the reason the REMS failed to prevent the pregnancy exposure; the root cause analysis should include patient interviews as a component. Include the protocol utilized to conduct the root cause analysis
- d. Overall summary and discussion of whether the data warrants further detailed assessment, labeling changes, and/or communication.

## **Knowledge**

### **5. Evaluation of Knowledge of the Qsymia REMS and Risks of Qsymia**

- a. An assessment of patients of reproductive potential's understanding of:
  - i. Increased risk of embryo-fetal toxicity with major congenital malformations, including but not limited to cleft lip and/or cleft palate (oral clefts) and of being small for gestational age (SGA) in a fetus exposed to Qsymia during the first trimester of pregnancy
  - ii. Importance of pregnancy prevention for patients of reproductive potential receiving Qsymia therapy
  - iii. Need to promptly discontinue Qsymia therapy in the event of a pregnancy
  - iv. The receipt, reading, and understanding by patients of reproductive potential of the Qsymia Medication Guide and Risk of Birth Defects with Qsymia patient brochure
  - v. Patients of reproductive potential receipt of counseling about pregnancy

prevention and effective contraceptive use including:

- 1) Counseling provider (i.e., prescriber, office nurse, pharmacist)
- 2) Duration of time spent counseling
- 3) Frequency of patient counseling (each visit while receiving Qsymia; first time prescribed Qsymia)

b. An assessment of pharmacists' understanding of:

- i. Increased risk of embryo-fetal toxicity with major congenital malformations, including but not limited to cleft lip and/or cleft palate (oral clefts), and of being small for gestational age (SGA) in a fetus exposed to Qsymia during the first trimester of pregnancy
- ii. Importance of pregnancy prevention for patients of reproductive potential receiving Qsymia therapy
- iii. Need to promptly discontinue Qsymia therapy in the event of a pregnancy
- iv. Assessment of pharmacists' awareness and understanding of the need to provide a Medication Guide and Risk of Birth Defects with Qsymia patient brochure with every Qsymia prescription dispensed

### **Overall Assessment of REMS Effectiveness**

6. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy is meeting the goal or whether one or more such goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

- a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
- b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
- c) *If the new indication for use introduces unexpected risks:* A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

- d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.
- e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
- f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications, provide a rationale for why the REMS does not need to be modified.*

If the methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted methodology, you should update the REMS supporting document to include specific methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

Prominently identify the submission containing the methodology with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 022580 REMS ASSESSMENT METHODOLOGY PROTOCOL REVIEW**  
(insert concise description of content in bold capital letters, e.g.,  
**SURVEY METHODOLOGIES, AUDIT PLAN, NONCOMPLIANCE PLAN, DRUG  
USE STUDY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block

or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**NDA 022580 REMS ASSESSMENT**

*or*

**NEW SUPPLEMENT FOR NDA 022580/S-000  
CHANGES BEING EFFECTED IN 30 DAYS  
PROPOSED MINOR REMS MODIFICATION**

*or*

**NEW SUPPLEMENT FOR NDA 022580/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED MAJOR REMS MODIFICATION**

*or*

**NEW SUPPLEMENT FOR NDA 022580/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING  
CHANGES SUBMITTED IN SUPPLEMENT 000**

*or*

**NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR NDA 022580/S-000  
REMS ASSESSMENT  
PROPOSED REMS MODIFICATION (if included)**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

**REMS REVISIONS FOR NDA 022580**

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

## **SUBMISSION OF REMS DOCUMENT IN SPL FORMAT**

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For more information on submitting REMS in SPL format, please email [FDAREMSwebsite@fda.hhs.gov](mailto:FDAREMSwebsite@fda.hhs.gov).

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplemental application, you are exempt from this requirement.

## **PATENT LISTING REQUIREMENTS**

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

## **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Martin White, M.S., Regulatory Project Manager, at (240) 402-6018.

Sincerely,

*{See appended electronic signature page}*

Monika Houstoun, Pharm.D., M.P.H.  
Deputy Director for Safety  
Division of Diabetes, Lipid Disorders, and Obesity  
Office of Cardiology, Hematology,  
Endocrinology, and Nephrology  
Office of New Drugs  
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information (version approved with NDA 022580/S-031 on March 6, 2026)
- Medication Guide (included in REMS enclosure)
- REMS

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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MONIKA A HOUSTOUN  
06/29/2026 04:14:01 PM