NDA 022580/S-025

SUPPLEMENT APPROVAL

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

Dear Maryam Azizi:

Please refer to your supplemental new drug application (sNDA) dated and received November 15, 2023, 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 Prior Approval sNDA provides for the following revisions to the Qsymia Prescribing Information:

- Editorial revisions to the indication statement in Section 1, *Indications and Usage*.
    - Revised Sections 2.1, *Patient Selection*; 8.4, *Pediatric Use*; 9.2, *Abuse*; and 12.1, *Mechanism of Action* to align with revisions to the indication statement in Section 1.
- Updates to Section 2.2, *Recommended Dosage and Administration*, Section 2.4, *Recommended Dosage in Patients with Renal Impairment, and* Section 2.5, *Recommended Dosage in Patients with Hepatic Impairment* to be consistent with the FDA guidance for industry, *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products – Content and Format.*[1]
- Updates based on data from study OB-409 entitled: "A Multicenter, Randomized, Double-Blind Study to Compare the Effects of VI-0521, Phentermine, and Placebo on Ambulatory Blood Pressure in Overweight or Obese Subjects."
    - Deleted Sections 5.2, *Increase in Heart Rate*
    - Updates to Sections 6.1, *Clinical Trial Experience*
    - Updates to 12.2, *Pharmacodynamics*
- Deleted Section 5.10, *Risk of Hypoglycemia in Patients with Type 2 Diabetes Mellitus on Antidiabetic Therapy*

[1] 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.

- Deleted Section 5.11, *Risk of Hypoglycemia in Patients with Antihypertensive Medications*
- Added America's Poison Centers in Section 10 *Overdosage*
- Revised the Medication Guide for consistency with the Prescribing Information. Additional revisions were made to reduce redundancy, to make patient information more consistent and concise, and to include the information necessary for patients to safely take their medication.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling with the minor editorial revision listed below and reflected in the enclosed labeling:

- Updated the revision date of the Prescribing Information and Medication Guide to reflect supplement approval.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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.[2] 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 the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.

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

[2] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 application, you are exempt from this requirement.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

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).

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[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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, contact Martin White, MS, Regulatory Project Manager, at 240-402-6018.

Sincerely,

{See appended electronic signature page}

John Sharretts, M.D.
Director
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
  - Medication Guide

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.

/s/

JOHN M SHARRETTS
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