NDA 021687/S-061
NDA 021687/S-064
NDA 021687/S-065

SUPPLEMENT APPROVAL

Organon LLC, a subsidiary of Organon & Co.
Attention: Mini Chen
Associate Principal Scientist, Regulatory Liaison
30 Hudson Street, Floor 33
Jersey City, NJ 07302

Dear Mini Chen:

Please refer to your supplemental new drug applications (sNDAs) and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Vytorin (ezetimibe and simvastatin) tablets.

Supplement 061

This Prior Approval sNDA, dated and received May 15, 2018, provides for updates to the Vytorin Prescribing Information (PI) to comply with the Pregnancy and Lactation Labeling Rule (PLLR).

Supplement 064

This Prior Approval sNDA, dated and received November 5, 2021, provides for the addition of lichen planus, to section 6.2 *Postmarketing Experience* of the Vytorin PI.

Supplement 065

This Prior Approval sNDA, dated and received February 21, 2023, provides for the addition of myasthenia gravis, including ocular myasthenia, to section 6.2 *Postmarketing Experience* of the Vytorin PI and the Patient Package Insert.

In addition, the following revision were made throughout the PI:

- Updates to Section 1 – *Indications and Usage,* to modernize the language to align with current labeling practice:
  - Added simvastatin cardiovascular outcomes data and indication
  - The heterozygous familial hypercholesterolemia (HeFH) indication was revised to include use of ezetimibe in combination with a statin in pediatric patients 10 years and older.

    - The homozygous familial hypercholesterolemia (HoFH) indication was revised to clarify use of Vytorin in adults with HoFH.
    - Removal of non-LDL-C parameters from the indications described above
    - Removal of Limitations of Use statement
- Updates to Section 2 – *Dosage and Administration,* to be consistent with current labeling practice
- Revisions to Section 4 – *Contraindications,* to remove contraindications for use during Pregnancy and Lactation and to modify the contraindication for use in patients with hepatic disease.
- Revisions to Section 5.2 – *Warnings and Precautions,* Section on Immune Mediated Necrotizing Myopathy to remove "Consider risk of IMNM carefully prior to initiation of a different statin. If therapy is initiated with a different statin, monitor for signs and symptoms of IMNM.", add "There have been postmarketing reports of recurrence of signs and symptoms of IMNM when the same or a different statin was administered."
- Associated revisions to Section 8 – *Use in Special Populations*
- Removed *Section 13.2, Animal Toxicology and Pharmacology,* based on the availability of sufficient human data to address the clinical relevance of these findings.
- Updates to Section 14 – *Clinical Studies*, the clinical trial information for pediatric patients with HeFH was moved from Section 8.4 to Section 14 and the trial data describing simvastatin cardiovascular outcomes trial results in patients treated with simvastatin was added to the section.
- Revisions to Section 17 – *Patient Counseling Information*
- Extensive edits made throughout the label to update and modernize with current labeling guidances and practices.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert), 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*.[2]

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).

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.

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

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, 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
  - Patient Package Insert

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
02/08/2024 02:51:37 PM