NDA 021995/S-047
NDA 022044/S-048
NDA 202270/S-022

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Merck Sharp & Dohme Corp.
Attention: Lou Ann Eader, Ph.D.
Director, Global Regulatory Affairs
351 N. Sumneytown Pike
P. O. Box 1000, UG2D-44
North Wales, PA 19454-1099

Dear Dr. Eader:

Please refer to your supplemental new drug applications (sNDAs) dated June 4, 2020, received June 4, 2020, and your amendments, submitted under section 505(b) and pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Januvia (sitagliptin) tablets, Janumet (sitagliptin and metformin HCl) tablets, and Janumet XR (sitagliptin and metformin HCl extended-release) tablets.

These Prior Approval supplemental new drug applications provide for:

NDA 21995/S-047 for Januvia
Changes to the Prescribing Information and Medication Guide based on the results of Protocol 083, entitled "A Phase III, Multicenter, Double-Blind, Randomized, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of Sitagliptin in Pediatric Patients with Type 2 Diabetes Mellitus with Inadequate Glycemic Control."

NDA 022044/S-048 for Janumet
Changes to the Prescribing Information and Medication Guide based on the results of Protocol 170, entitled "A Phase III, Multicenter, Double-blind, Randomized, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of MK-0431A (A Fixed-Dose Combination Tablet of Sitagliptin and Metformin) in Pediatric Patients with Type 2 Diabetes Mellitus with Inadequate Glycemic Control on Metformin Therapy (Alone or in Combination with Insulin)."

NDA 202270/S-022 for Janumet XR
Changes to the Prescribing Information and Medication Guide based on the results of Protocol 289, entitled "A Phase III Multicenter, Double-blind, Randomized, Placebo-controlled Clinical Trial to Evaluate the Safety and Efficacy of MK-0431A XR (a Fixed-Dose Combination Tablet of Sitagliptin and Extended-Release Metformin) in Pediatric

Patients with Type 2 Diabetes Mellitus with Inadequate Glycemic Control on Metformin Therapy (Alone or in Combination with Insulin)."

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 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*.[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).

[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.

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 these supplemental applications, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

The supplemental application for NDA 021995 contained the final report for the following postmarketing requirement listed in the October 16, 2006, approval letter for NDA 021995.

PMR 224-1 Deferred pediatric study under PREA for the treatment of type 2 diabetes in pediatric patients ages 11 to 16, inclusive.

The supplemental application for NDA 022044 contained the final report for the following postmarketing requirement listed in the March 30, 2007, approval letter for NDA 022044.

PMR 856-1 Deferred pediatric study under PREA for the treatment of type 2 diabetes in pediatric patients ages 11 to 16, inclusive.

The supplemental application for NDA 202270 contained the final report for the following postmarketing requirement listed in the February 2, 2012, approval letter for NDA 202270.

PMR 1802-4 A 54-week, randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of JANUMET XR versus metformin extended-release in pediatric patients who are inadequately controlled on metformin immediate release.

We have reviewed your submissions and conclude that the above requirements were fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our October 16, 2006, March 30, 2007, and February 2, 2012, approval letters.

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]

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 Michael Oyewole, Regulatory Project Manager, at (301) 796-3897.

Sincerely,

{See appended electronic signature page}

Patrick Archdeacon, M.D.
Associate Director for Therapeutics
Division of Diabetes, Lipid Disorders, and Obesity
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Center for Drug Evaluation and Research

[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

ENCLOSURES:

- Content of Labeling for Januvia (sitagliptin) tablets
  - Prescribing Information
  - Medication Guide
- Content of Labeling for Janumet (sitagliptin and metformin HCl) tablets
  - Prescribing Information
  - Medication Guide
- Content of Labeling for Janumet XR (sitagliptin and metformin HCl extended-release) tablets
  - Prescribing Information
  - Medication Guide

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