DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202270

NDA APPROVAL

Merck Sharp & Dohme Corp.
Attention: Richard J. Swanson, Ph.D.
Senior Director, Regulatory Affairs
P.O. Box 1000, UG2C-50
North Wales, PA 19454-1099

Dear Dr. Swanson:

Please refer to your New Drug Application (NDA) dated September 23, 2010, received September 23, 2010, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for JANUMET XR (sitagliptin/metformin hydrochloride extended-release) fixed-dose combination tablets, 100 mg/1000 mg, 50 mg/500 mg, and 50 mg/1000 mg.

We acknowledge receipt of your amendments dated September 30, November 11 and 12, December 16 and 23, 2010, and January 10 (2), January 21, March 25, April 11, 13, 27, and 29, May 6 (2), 18, 27, and 31, June 3, 22, and 30, July 1 (2), 11, 12 (2), 18, and 21 (2), August 3 and 16, and September 7, 2011, and January 26 and 31, 2012. The August 3, 2011, submission constituted a complete response to our July 22, 2011, action letter.

This new drug application provides for the use of JANUMET XR as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both sitagliptin and metformin extended-release is appropriate.

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 text.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and text for the Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202270**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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.

We are waiving the pediatric study requirement for ages 0 to 9 years (inclusive) because the necessary studies are impossible or highly impractical. This is because there are too few children in this age range with type 2 diabetes mellitus to study.

We are deferring submission of your pediatric study for ages 10 to 17 years (inclusive) for this application because the product is ready for approval for use in adults and pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

PMR 1802-1: A pharmacokinetic study of JANUMET XR in pediatric patients 10 through 17 years of age (inclusive) with type 2 diabetes mellitus.

Final Protocol Submission:	by June 1, 2012
Trial Completion:	by December 1, 2013
Final Report Submission:	by June 1, 2014

PMR 1802-2: A 54-week, randomized, double-blind placebo-controlled trial to evaluate the efficacy and safety of JANUMET XR vs. metformin in pediatric patients who are inadequately controlled on diet and exercise. You must also evaluate whether pediatric patients can safely swallow JANUMET XR over the course of the trial.

Final Protocol Submission:	by June 1, 2012
Trial Completion:	by September 1, 2016
Final Report Submission:	by March 1, 2017

Submit the protocols to your IND 101964, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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 Raymond Chiang, Regulatory Project Manager, at (301) 796-1940.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:
Package Insert
Medication Guide
Container Label – 50 mg/500 mg, 14 tablet bottle (sample)
Container Label - 50 mg/500 mg, 60 tablet bottle
Container Label – 50 mg/500 mg, 180 tablet bottle

Container Label – 50 mg/500 mg, 1000 tablet bottle
Container Label – 50 mg/1000 mg, 60 tablet bottle
Container Label – 50 mg/1000 mg, 14 tablet bottle (sample)
Container Label – 50 mg/1000 mg, 180 tablet bottle
Container Label – 50 mg/1000 mg, 1000 tablet bottle
Container Label – 100 mg/1000 mg, 30 tablet bottle
Container Label – 100 mg/1000 mg, 7 tablet bottle (sample)
Container Label – 100 mg/1000 mg, 90 tablet bottle
Container Label – 100 mg/1000 mg, 1000 tablet bottle
Carton Label – 50 mg/500 mg tablets (sample)
Carton Label – 50 mg/1000 mg tablets (sample)
Carton Label – 100 mg/1000 mg tablets (sample)

DOCKET ALARM

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