DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 200678

NDA APPROVAL

Bristol-Myers Squibb Company
Attention: Pamela J. Smith, M.D.
Group Director, Global Regulatory Strategy
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Smith:

Please refer to your New Drug Application (NDA) dated December 29, 2009, received December 29, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Kombiglyze XR (saxagliptin/metformin hydrochloride extended-release) tablets, 5 mg saxagliptin/500 mg metformin hydrochloride extended-release, 5 mg saxagliptin/1000 mg metformin hydrochloride extended-release, and 2.5 mg saxagliptin/1000 mg metformin hydrochloride extended-release.

We acknowledge receipt of your amendments dated January 12, February 5, March 10 and 23, April 23, 26, 28, and 29, May 25, 27, and 28, June 16, July 20 and 23, August 3 and 13 (2), September 1, 21, 22, 24 (2), 28, 29 (2), and 30, October 6, 7, 8, 12, 19, 22, 27, and 28, and November 1, 2010.

This new drug application provides for the use of Kombiglyze XR (saxagliptin/metformin hydrochloride extended-release) tablets as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin 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.

Sufficient stability data have been submitted to support a 21-month expiration dating period for the bottle presentations and a 15-month expiration dating period for the blister presentations.

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, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert and the patient package insert). 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 carton and immediate container labels submitted on October 22, 2010, 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 200678**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) 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(s) 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 impracticable (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 16 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act 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 Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

PMR 1703-1: A clinical pharmacology study in pediatric patients with type 2 diabetes comparing the pharmacokinetics of Kombiglyze XR to co-administered saxagliptin and metformin immediate-release tablets. As part of this study, you must evaluate whether pediatric patients can safely swallow the large Kombiglyze XR tablets.

Final Protocol Submission:	by October 31, 2011
Trial Completion:	by January 31, 2013
Final Report Submission:	by December 2013

PMR 1703-2: A 52-week, randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of saxagliptin vs. placebo, both as add-on therapy to metformin in pediatric patients with inadequate glycemic control on metformin alone. Approximately one-half of the patients must be on metformin extended-release therapy at the time of randomization to add-on saxagliptin vs. add-on placebo. As part of this study, you must evaluate whether pediatric patients can safely swallow the large metformin extended-release tablets.

Final Protocol Submission:	by June 30, 2011
Trial Completion:	by April 30, 2015
Final Report Submission:	by December 31, 2015

Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessment(s)**".

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.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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, Consumer Safety Officer, at (301) 796-1940.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:
- Package Insert
- Patient Package Insert
- Container Label – 2.5 mg/1000mg, 6 tablet blister card (sample)
- Container Label – 2.5mg/1000mg, 60 tablet bottle
- Container Label – 2.5 mg/1000mg, 500 tablet bottle
- Container Label – 5mg/500mg, 7 tablet blister card (sample)
- Container Label – 5mg/500mg, 30 tablet bottle
- Container Label – 5 mg/1000mg, 7 tablet blister card (sample)

Container Label – 5 mg/ 1000mg, 30 tablet bottle
Container Label – 5mg/1000mg, 90 tablet bottle
Container Label – 5 mg/1000mg, 500 tablet bottle
Carton Label - 2.5 mg/1000mg, 6 tablets (sample)
Carton Label – 5mg/500mg, 7 tablets (sample)
Carton Label – 5mg/1000mg, 7 tablets (sample)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARY H PARKS
11/05/2010