CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-178

APPROVAL LETTER

Food and Drug Administration
Rockville MD 20857

NDA 21-178

Bristol-Myers Squibb
Attention: Warren C. Randolph
Director, Regulatory Science
PO Box 5400
Princeton, New Jersey 08543-5400

JUL 31 2000

Dear Mr. Randolph:

Please refer to your new drug application (NDA) dated September 30, 1999, received September 30, 1999, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Glucovance (glyburide and metformin hydrochloride tablets).

We acknowledge receipt of your submissions dated October 8 and 28, November 5 and 24, and December 2, 7, 16, and 24, 1999, and January 27 and 28, February 14, April 28, May 18, June 12, 16, and 23, and July 5, 13 (4), 24, 26 (2), 27, 28 (2), and 31, 2000.

This new drug application provides for the use of Glucovance (glyburide and metformin hydrochloride tablets) in 1.25 mg / 250 mg, 2.5 mg / 500 mg, and 5 mg / 500 mg strengths for the following two indications:

1. As initial therapy, as an adjunct to diet and exercise, to improve glycemic control in patients with type 2 diabetes whose hyperglycemia cannot be satisfactorily managed with diet and exercise alone.

2. As second-line therapy when diet, exercise, and initial treatment with a sulfonylurea or metformin do not result in adequate glycemic control in patients with type 2 diabetes.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the attached labeling (package insert and patient package insert) and the immediate container and carton labels submitted July 26, 2000. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-178." Approval of this submission by FDA is not required before the labeling is used.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55. We are deferring submission of your pediatric studies until July 31, 2002. However, your pediatric drug development plan is under review, and we will notify you of its adequacy by September 30, 2000.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call William C. Koch, R.Ph., Regulatory Project Manager, at (301) 827-6412.

Sincerely

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John K. Jenkins, M.D.
Acting Director
Division of Metabolic
and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research