CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-108

Approval Letter

ANDA 75-108

DEC 17 1999

Mylan Pharmaceuticals, Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

Dear Sir:

This is in reference to your abbreviated new drug application dated April 7, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Nifedipine Extended-release Tablets, 30 mg.

Reference is also made to our tentative approval letter dated March 15, 1999, and to your amendments dated December 8, 1997; and June 1, October 14, and December 3, 1999.

The listed drug product (RLD) referenced in your application, Procardia XL Tablets, 30 mg, of Pfizer Laboratories, is subject to periods of patent protection which expire on November 25, 2000 (U.S. Patent No. 4,327,725), September 16, 2003 (U.S. Patents 4,612,008, 4,765,989, and 4,783,337), and November 23, 2010 (U.S. Patent No. 5,264,446, the '446 patent). Your application contains a patent certifications under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, sale, offer for sale or importation of Nifedipine Extended-release Tablets, 30 mg, will not infringe on any of these patents, or that the patents are invalid, unenforceable, or will not be infringed. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated new drug application shall be made effective immediately unless an action is brought before the expiration of forty-five (45) days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified the Agency that Mylan Pharmaceuticals, Inc. (Mylan) has complied with the requirements of Section 505(j)(2)(B) of the Act, and that a patent infringement suit involving the '446 patent was initiated against Mylan in the United States District Court for the Western District of Pennsylvania (Bayer AG, Bayer Corporation and Pfizer Inc. v. Mylan Laboratories, Inc. and Mylan Pharmaceuticals, Inc., Civil Action No. 97-1309).

You have also advised the Agency that the 30-month period provided for under section 505(j)(5)(B)(iii) since the date of receipt of the 45-day notice by the NDA and patent holders as required under section 505(j)(2)(B)(i) of the Act expired on December 16, 1999.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Nifedipine Extended-release Tablets, 30 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Procardia® XL Tablets, 30 mg, of Pfizer Laboratories).

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The "interim" dissolution test and tolerances are:

> The dissolution testing should be conducted in 250 mL of SGF, with 0.25% TWEEN 80 for the first hour; then 250 ml of 0.01M phosphate buffer, pH 6.8 with 0.25% TWEEN 80 between 2 and 24 hrs, both at 37°C using USP Apparatus (III) at 20 dpm. The test product should meet the following tentative specifications:
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> | | |
> |---|---|
> | 1 hr | NMT 5% |
> | 2 hrs | NMT 15% |
> | 8 hrs | 40-65% |
> | 12 hrs | 65-90% |
> | 24 hrs | NLT 80% |

The "interim" dissolution test and tolerances should be finalized by submitting dissolution data for the first three production size batches in a supplemental application. A "Special Supplemental-Changes Being Effected" (zero) should be submitted if no revisions to the interim specifications are proposed or if the final specifications are tighter than the interim specifications. In all other instances a Prior Approval supplement should be submitted.

Under Section 506(A) of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy, which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/S/

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

12/17/99

ANDA 75-108

MAR 15 1999

Mylan Pharmaceuticals, Inc.
Attention: Frank Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

Dear Sir:

This is in reference to your abbreviated new drug application dated April 7, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Nifedipine Extended-release Tablets, 30 mg.

Reference is also made to your amendments dated May 19, May 21, May 27, July 18, July 25, September 17, September 25, October 31, November 7, and December 8, 1997; March 12, April 21, September 10, and December 23, 1998; and January 5, and February 17, 1999.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved.** This determination is based upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention. This letter does not address notice issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The listed drug product referenced in your application, Procardia XL Extended-release Tablets of Pfizer Laboratories, is subject to periods of patent protection which expire on September 16, 2003 (U.S. patents 4,612,008 [the'008 patent], 4,783,337 [the'337 patent], and 4,765,989 [the'989 patent]), November 23, 2010 (U.S. patent 5,264,446 [the '446 patent]), and November 25, 2000, (U.S. patent 4,327,725 [the '725 patent]), respectively. Your application contains patent certifications under Section

505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, sale, offer for sale, or importation of this drug product will not infringe on any of these patents, or that the patents are invalid, unenforceable, or will not be infringed. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated new drug application shall be made effective immediately unless an action is brought before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified FDA that Mylan Pharmaceuticals, Inc. (Mylan) has complied with the requirements of Section 505(j)(2)(B) of the Act. However, you have also notified the agency that litigation is currently underway in the United States District Court for the Western District of Pennsylvania involving a challenge to the '446 patent (Bayer AG, Bayer Corporation and Pfizer, Inc. v Mylan Laboratories Inc., and Mylan Pharmaceuticals Inc., Civil Action No. 97-1309). Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii) since the date of receipt of the 45-day notice required under section 505(j)(2)(B)(i), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or,

   b. the date of court decision [505(j)(5)(B)(iii)(I), (II), or (III)], which has been interpreted by the Agency to mean the date of the final order or judgement of that court from which no appeal can be or has been taken, or,

   c. the '446 patent has expired, and

2. The Agency is assured there is no new information that would affect whether final approval should be granted.

Because the Agency is granting a tentative approval for this application, when you believe that your application may be considered for final approval, you must amend your application to notify the Agency whether circumstances have or have not arisen that may affect the effective date of final approval. Your amendment must provide:

1. A copy of a final order or judgement from which no appeal may be taken (which might not be the one from the district court), or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information, and

2. a. updated information related to labeling or chemistry, manufacturing and controls data, or any other change in the conditions outlined in this abbreviated application, or

   b. a statement that no such changes have been made to the application since the date of tentative approval.

Any changes in the conditions outlined in this abbreviated application and the status of the manufacturing and testing facilities' compliance with current good manufacturing procedures (CGMPs) are subject to Agency review before final approval of the application will be made.

In addition to, or instead of, the amendments referred to above, the Agency may, at any time prior to the final date of approval, request that you submit amendments containing the information requested above.

Failure to submit either or both amendments may result in rescission of this tentative approval determination, or delay in issuance of the final approval letter.

The drug product that is the subject of this abbreviated application may not be marketed without final Agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug before the effective final approval date is prohibited under section 501 of the Act. Also, until the Agency issues the final approval letter, this drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list.

The amendment should be designated as a MINOR AMENDMENT in your cover letter. Before you submit the amendment, please contact Timothy Ames, Project Manager, at (301) 827-5849, for further instructions.

Sincerely yours,

/S/ 3/15/99

Roger L. Williams, M.D.
Deputy Center Director for
Pharmaceutical Science
Center for Drug Evaluation and Research