CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-140

Approval Letter

ANDA 75-140

SEP 28 1998

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

Dear Sir:

Reference is made to your abbreviated new drug application dated June 6, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Terazosin Hydrochloride Capsules, 1 mg (base), 2 mg (base), 5 mg (base), and 10 mg (base).

Reference is also made to your amendments dated September 3, 1997; and January 30, February 6 and 24, July 16, and August 5, 1998.

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 of the facilities used in the manufacturing and testing of the drug product) and is, therefore, 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)(4)(B)(iv) of the Act.

The listed drug product referenced in your application is subject to periods of patent protection which expire on February 17, 2000 (patent 4,251,532), June 29, 2010 (patent 5,212,176), and April 29, 2013 (patents 5,504,207; 5,412,095; and 5,294,615), respectively. Your application contains certifications to each of these patents under Section 505(j)(2)(A)(vii)(IV) of the Act stating that to the best of Mylan's knowledge the patents are invalid, unenforceable or that your manufacture, use, sale, or offer for sale, or importation of Terazosin Hydrochloride Capsules will not infringe on the patents. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement of the patent(s) which are the subject of the certifications before the expiration of forty-five days from the

date the notice provided under paragraph (2)(B)(i) is received. However, you have notified FDA that litigation is underway in the United States District Court for the Northern District of Illinois, Eastern Division, involving a challenge to patent 5,504,207 (the '207 patent) (Abbott Laboratories, an Illinois Corporation, v. Mylan Pharmaceuticals Inc., Civil Action No. 97-C-5450 and 98-C-1280). 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 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 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, these drug products will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list.

Validation of the regulatory methods has not been completed. It is the policy of the Office not to withhold approval until the validation is complete. We acknowledge your commitment to satisfactorily resolve any deficiencies which may be identified.

The amendment should be designated as a MINOR AMENDMENT in your cover letter. Before you submit the amendment, please contact Joseph Buccine, Project Manager, at (301) 827-5848, for further instructions.

Sincerely yours,

/S/ 9-25-98

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

ANDA 75-140

FEB 11 2000

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 June 6, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Terazosin Hydrochloride Capsules, 1 mg (base), 2 mg (base), 5 mg (base), and 10 mg (base).

Reference is also made to our Tentative Approval letter dated September 28, 1998, and to your amendments dated September 3, 1997; January 30, and February 24, 1998; and February 3, 2000.

As noted in the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations (19th Edition)", also known as the "Orange Book", the listed drug product (RLD) referenced in your application, Hytrin Capsules of Abbott Laboratories, is subject to periods of patent protection which expire on February 17, 2000 (U.S. Patent No. 4,251,532), June 29, 2010 (U.S. Patent No. 5,212,176), and April 29, 2013 (U.S. Patent Nos. 5,504,207; 5,412,095; and 5,294,615). Your application contains Paragraph IV Certifications to each of these patents under Section 505(j)(2)(A)(vii)(IV) of the Act stating that to the best of Mylan's knowledge the patents are invalid, unenforceable or that your manufacture, use, sale, or offer for sale, or importation of Terazosin Hydrochloride Capsules will not infringe on the patents. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement of the patent(s) which are the subject of the certifications before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. You informed us that Abbott Laboratories initiated a patent infringement action against you in the United States District Court for the Northern District of Illinois, Eastern Division, involving a challenge to U.S. Patent No. 5,504,207 only (Abbott Laboratories v. Mylan Pharmaceuticals, Inc., Civil Action No. 97-C-5450 and 98-C-1280). We note that no action was brought against Mylan Pharmaceuticals, Inc. (Mylan) by

either the patent holder or NDA holder with regard to the other 4 patents listed in the Paragraph IV Certifications. Subsequent to our issuance of the tentative approval letter, you informed us that Mylan prevailed in the both the district court and in the United States Court of Appeals for the Federal Circuit with respect to the finding that U.S. Patent No. 5,504,207 is invalid.

Furthermore, the Act provides that approval of an abbreviated application that contains a certification described in Section 505(j)(2)(A)(vii)(IV) (a "Paragraph IV Certification"), and that is for a drug product for which a previous abbreviated application has been submitted which also contains a Paragraph IV Certification, shall be made effective not earlier than one hundred and eighty days after:

1. the date the Secretary receives notice of the first commercial marketing of the drug product under the previous application, or

2. the date of a final decision of a court holding the patent(s) which is the subject of the certification to be invalid or not infringed, whichever event occurs first {Section 505(j)(5)(B)(iv)}.

As noted in "Approved Drug Products with Therapeutic Equivalence Evaluations", the "Orange Book", an abbreviated new drug application for this drug product was approved for Geneva Pharmaceuticals Inc. (Geneva) on December 31, 1998. This was the first application received by the Agency for this drug product containing a Paragraph IV Certification. Consequently, Geneva became eligible for 180 days of market exclusivity commencing on the date of first commercial marketing. According to the "Orange Book", Geneva's market exclusivity expired on February 9, 2000.

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 Terazosin Hydrochloride Capsules, 1 mg (base), 2 mg (base), 5 mg (base), and 10 mg (base) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Hytrin® Capsules 1 mg (base), 2 mg (base), 5 mg (base), and 10 mg (base), respectively, of Abbott Laboratories). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A 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

2/11/00