

February 8, 2002

TEVA Pharmaceuticals USA
Attention: Philip Erickson
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

Dear Sir:

This is in reference to your abbreviated new drug application dated November 20, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Quinapril Hydrochloride Tablets, 5 mg, 10 mg, 20 mg, and 40 mg.

Reference is also made to your amendments dated June 10, 1999; August 16, October 2, October 12, and November 27, 2001; and January 18, 2002.

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). The determination 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, Accupril Tablets of Parke Davis, is subject to periods of patent protection. U.S. Patent No. 4,344,949 (the '949 patent) expires on October 3, 2002. Your application contains a Paragraph III Certification under Section 505(j)(2)(A)(vii)(III) of the Act stating that you will not market this product prior to the expiration of this patent. Your application also contains patent statements under Section 505(j)(2)(A)(viii) of the Act

indicating that U.S. Patent Nos. 5,684,016 and 5,747,504 (expiring November 4, 2014 and April 10, 2005, respectively) are method of use patents, and that these two patents do not claim any of the indications for which you are seeking approval. In addition, your application contains a Paragraph IV Certification to U.S. Patent No. 4,743,450 (the '450 patent) under Section 505(j)(2)(A)(vii)(IV) of the Act stating that the '450 patent which is to expire on February 24, 2007, is invalid. 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 against TEVA Pharmaceuticals USA (TEVA) as a result of the Paragraph IV Certification. Such action must be brought against TEVA prior to the expiration of forty-five (45) days from the date the notice provided by TEVA under paragraph (2)(B)(i) is received by the patent and new drug application (NDA) holders. You have notified the agency that TEVA complied with the requirements of Section 505(j)(2)(B) of the Act, and that as a result of this action Parke Davis initiated litigation in the United States District Court for the District of New Jersey the involving a challenge to the '450 patent [Warner Lambert Company v. TEVA Pharmaceuticals USA, Civil Action No. 99-922(DRD)]. You have also notified the agency that the 30-month period identified in Section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your application as a result of this litigation, has expired. Therefore, final approval cannot be granted until the '949 patent expires, currently October 3, 2002.

In order to reactivate your application prior to final approval, please submit a MINOR AMENDMENT - FINAL APPROVAL REQUESTED between 60 to 90 days prior to the date you believe that this application is eligible for final approval. This amendment should inform the agency of the legal basis for such approval and should also include:

1. If applicable, 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), settlement agreement between the parties, licensing agreement between you and the patent holder, or any other relevant information, and
2. a. updated information related to final-printed 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.

Additional amendments not requesting final approval but providing for significant changes to the application should be submitted in accord with the Office of Generic Drugs amendment classification system. These will be classified and reviewed according to established office policy. In addition to, or instead of the amendment requested above, the agency may request at any time prior to the final date of approval that you submit an amendment containing the requested information.

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.

Failure to submit amendments as requested 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 requesting final approval should be designated clearly as a MINOR AMENDMENT - FINAL APPROVAL REQUESTED in your cover letter. Before you submit the amendment, please contact Timothy Ames, Project Manager, at 301-827-5848, for further instructions.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research