DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 079135

Glenmark Generics Inc., USA
U.S. Agent for: Glenmark Generics Ltd.
Attention: William McIntyre, Ph.D.
Executive Vice President, Regulatory Affairs
750 Corporate Drive
Mahwah, NJ 07430

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated July 24, 2007, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 1 mg/240 mg, 2 mg/180 mg, 2 mg/240 mg and 4 mg/240 mg.

Reference is made to the tentative approval letter issued by this office on January 21, 2010, and to your amendments dated July 25, and October 7, 2008; March 24, 2009; and February 5, February 23, and March 2, 2010.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. However, because of the patent issue explained below, we are unable to approve your Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 1 mg/240 mg, 2 mg/180 mg and 2 mg/240 mg, at this time. Therefore, only your Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 4 mg/240 mg, is approved.

The reference listed drug (RLD) upon which you have based your ANDA, Abbott's Tarka Tablets, is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent No. 5,721,244 (the '244 patent) expires on February 24, 2015.

Your ANDA contains a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act stating that the '244 patent is invalid, unenforceable, or will not be infringed by your

manufacture, use, or sale of Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 1 mg/240 mg, 2 mg/180 mg, 2 mg/240 mg and 4 mg/240 mg, under this ANDA. You notified the agency that Glenmark complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the '244 patent was brought against Glenmark within the statutory 45-day period in the United States District Court for the District of New Jersey [Sanofi-Aventis Deutschland GMBH, Aventis Pharma S.A., Abbott GMBH & Co. KG, and Abbott Laboratories v. Glenmark Generics Inc., USA and Glenmark Generics Limited. Civil Action No. 07-CV-05855 and 08-CV-01658].

Original #1 (4 mg/240 mg Strength) - Final Approval:

Although this litigation remains ongoing, the 30-month period identified in section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving you ANDA insofar as it pertains to Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 4 mg/240 mg, has expired. This strength is therefore approved.

With respect to 180-day generic drug exclusivity, we note that Glenmark was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the '244 patent. Therefore, with this approval, Glenmark is eligible for 180-days of generic drug exclusivity for Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 4 mg/240 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.

The Division of Bioequivalence has determined your Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 4 mg/240 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Tarka Tablets, 4 mg/240 mg, of Abbott Laboratories.

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The “interim” dissolution specifications are as follows:

Trandolapril: Dissolution testing should be conducted in 500 mL of water at 37°C, USP Apparatus 2 (paddle) at 50 rpm. The test product should meet the following "interim" specifications: Not less than (b) (4) (Q) of the labeled amount of trandolapril in the dosage form is dissolved in 60 minutes.

Verapamil: Dissolution testing should be conducted in 900 mL of gastric fluid (without pepsin) at pH 1.2 for the first hour, followed by intestinal fluid (without pancreatin) at pH 7.5 for 1-8 hours, USP Apparatus 2 (paddle) with Japanese sinkers, at 50 rpm and 37°C. The test product should meet the following "interim" specifications: 1 hr: (b) (4), 2 hr: (b) (4), 3.5 hr: (b) (4), 5 hr: NLT (b) (4) and 8 hr: Not less than (b) (4) of the labeled amount of verapamil in the dosage form is dissolved.

These "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement - Changes Being Effected" if there are no revisions to be made to the "interim" specifications, or if the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

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

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

Postmarketing reporting requirements for this ANDA 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.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in

draft or mock-up form, two copies of both the promotional materials and package insert directly 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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Within 14 days of the date of this letter, submit updated content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling. For administrative purposes, please designate this submission as "***Labeling/SPL Final for Approved ANDA 079135***".

Original #2 (2 mg/180 mg and 2 mg/240 mg) - Tentative Approval:

Your Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 2 mg/180 mg and 2 mg/240 mg, remain tentatively approved due to the unexpired 30-month stay of approval noted in our tentative approval letter of January 21, 2010. The stay of approval expires on May 26, 2010, for the 2 mg/180 mg and 2 mg/240 mg strengths.

To reactivate your ANDA prior to final approval of one or more of these strengths, please submit a **"FINAL APPROVAL REQUEST AMENDMENT TO ORIGINAL #2"** immediately upon receipt of this letter. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a **"FINAL APPROVAL REQUEST AMENDMENT TO ORIGINAL #2."**

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the application will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the application will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

Original #3 (1 mg/240 mg) - Tentative Approval:

Your Trandolapril and Verapamil Hydrochloride Extended-release Tablets, 1 mg/240 mg, remain tentatively approved due to the unexpired 30-month stay of approval noted in our tentative approval letter of January 21, 2010. The stay of approval expires on August 29, 2010, for the 1 mg/240 mg strength.

To reactivate your ANDA prior to final approval of your 1 mg/240 mg strength, please submit a **"FINAL APPROVAL REQUEST AMENDMENT TO ORIGINAL #3"** 90 days prior to the date you believe that it will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as

final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a **"FINAL APPROVAL REQUEST AMENDMENT TO ORIGINAL #3."**

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the application will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The three unapproved strengths of this drug product may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of these unapproved strengths before the final approval date(s) is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter(s), the unapproved strengths of this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

For further information on the status of this ANDA, or prior to submitting additional amendments, please contact Dat Doan, Project Manager, at (240) 276-8573.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-79135	ORIG-1	GLENMARK GENERICS LTD	TRANDOLAPRIL/VERAPAMIL
ANDA-79135	ORIG-2	GLENMARK GENERICS LTD	TRANDOLAPRIL/VERAPAMIL
ANDA-79135	ORIG-3	GLENMARK GENERICS LTD	TRANDOLAPRIL/VERAPAMIL

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

/s/

ROBERT L WEST
05/05/2010
Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.