DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 203821

ANDA APPROVAL

Glenmark Pharmaceuticals Inc., USA
U.S. Agent for Glenmark Pharmaceuticals Limited
750 Corporate Drive
Mahwah, NJ 07430
Attention: Kalpana Vanam
Vice President, Head of Regulatory Affairs, North America

Dear Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on December 19, 2011, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Nebivolol Tablets, 2.5 mg, 5 mg, 10 mg, and 20 mg.

Reference is also made to the complete response letter issued by this office on February 23, 2015, and to your amendments received on December 14, 2015; and March 7, May 20, June 22, and August 23, 2016.

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. Accordingly the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Nebivolol Tablets, 2.5 mg, 5 mg, 10 mg, and 20 mg to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Bystolic Tablets, 2.5 mg, 5 mg, 10 mg, and 20 mg of Forest Laboratories, LLC (Forest). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

The RLD upon which you have based your ANDA, Forest's Bystolic Tablets, 2.5 mg, 5 mg, 10 mg and 20 mg, is subject to a period of patent protection. The following patent and expiration date is currently listed in the Agency's publication titled *Approved Drug Products With Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
6,545,040 (the '040 patent)	December 17, 2021

Your ANDA contains a paragraph IV certifications to the '040 patent, under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Nebivolol Tablets, 2.5 mg, 5 mg, 10 mg, and 20 mg, under this ANDA. You have notified the Agency that Glenmark Pharmaceuticals Limited (Glenmark) complied with the requirements of section 505(j)(2)(B) of the FD&C Act and that litigation was initiated within the statutory 45-day period against Glenmark for infringement

of the ‘040 patent in the United States District Court for The Northern District Of Illinois [Forest Laboratories Holdings, Ltd. v. Glenmark Generics Inc., USA, Glenmark Generics Ltd., and Glenmark Pharmaceuticals Ltd., Civil Action No. 1:12-cv-05026]. You have also notified the Agency that this case was dismissed.

With respect to 180-day generic drug exclusivity, we note that Glenmark was one of the first ANDA applicants to submit a substantially complete ANDA with a paragraph IV certification for Nebivolol Tablets, 2.5 mg, 5 mg, 10 mg, and 20 mg. Therefore, with this approval, Glenmark may be eligible for 180 days of generic drug exclusivity for Nebivolol Tablets, 2.5 mg, 5 mg, 10 mg, and 20 mg. The Agency notes that Glenmark failed to timely obtain tentative approval of this ANDA under section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The Agency is not, however, making a formal determination at this time of Glenmark’s eligibility for 180-day generic drug exclusivity.

At least one first applicant remains eligible for 180 days of generic drug exclusivity for Nebivolol Tablets, 2.5 mg, 5 mg, 10 mg, and 20 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing by any first applicant, as identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date you begin commercial marketing.

Under section 506A of the FD&C 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 and 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 FD&C Act.

REPORTING REQUIREMENTS

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

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] 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 (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL

files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

The Electronic Common Technical Document (eCTD) is CDER's standard format for electronic regulatory submissions. Beginning May 5, 2017, ANDAs must be submitted in eCTD format and beginning May 5, 2018, drug master files must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: www.fda.gov/ectd.

Sincerely yours,

{See appended electronic signature page}

For Carol A. Holquist, RPh
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

Priya Shah

Digitally signed by Priya Shah
Date: 5/25/2017 11:16:41PM
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