NDA 210428

NDA APPROVAL

Sun Pharmaceutical Industries Limited
Attention: Mr. Ronak Patel
2 Independence way, Sun Pharmaceutical Industries, Inc.
Princeton, NJ 08540

Dear Mr. Patel:

Please refer to your new drug application (NDA) dated and received March 30, 2017, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Metoprolol Succinate Extended-Release 25 mg, 50 mg, 100 mg, and 200 mg Capsules.

We also refer to our approval letter dated January 26, 2018 in which we inadvertently left out the PREA Post Marketing Requirement for children with hypertension, from birth to 6 years old.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain January 26, 2018, the date of the original approval letter.

This new drug application provides for the use of Metoprolol Succinate Extended-Release Capsules for the treatment of:

- Hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions.
- Angina Pectoris.
- Heart Failure, to reduce the risk of cardiovascular mortality and heart-failure hospitalization in patients with heart failure.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the prescribing information). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*,

available at
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 210428**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for metoprolol succinate extended-release was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment, or prevention of a disease

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application for the Angina Pectoris and Heart Failure indications because necessary studies are impossible or highly impracticable to conduct in children.

Your deferred pediatric study required by section 505B(a) FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. This required study is listed below.

3638-1 Conduct a randomized, dose-ranging, double-blind, placebo-controlled, parallel group, multi-center clinical study with an open-label 52-week safety extension to evaluate efficacy, safety, tolerability and pharmacokinetics of metoprolol succinate extended release (ER) oral

dosage form in hypertensive pediatric subjects from birth to less than 6 years of age

Final Protocol Submission: 10/2019
Study Completion: 04/2026
Final Report Submission: 04/2027

Submit the protocol(s) to your IND 127963, with a cross-reference letter to this NDA.

Reports of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

This product is appropriately labeled for use in pediatric populations aged 6 to 17 years old with Hypertension. Therefore, no additional pediatric studies are needed at this time for this age group.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. 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 prescribing information, 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 20705-1266

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).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Maryam Changi, Regulatory Project Manager, at (240) 402-2725.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, MD, PhD
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

NORMAN L STOCKBRIDGE
01/26/2018 12:00:00 AM