

NDA 219373

**NDA APPROVAL**

Rubicon Research Private Limited  
c/o Advagen Pharma Limited  
Attention: Daliya Bharati  
Director – Regulatory Affairs and Intellectual Property  
50 Millstone Road, Building 200, Suite 180  
East Windsor, New Jersey 08520

Dear Daliya Bharati:

Please refer to your new drug application (NDA) received June 20, 2024 and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lopressor (Metoprolol Tartrate) Oral Solution.

This NDA provides for the use of Lopressor (Metoprolol Tartrate) Oral Solution for:

- 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.
- Long-term treatment of angina pectoris, to reduce angina attacks and to improve exercise tolerance.
- Treatment of hemodynamically stable patients with definite or suspected myocardial infarction, to reduce the risk of cardiovascular mortality when used in conjunction with intravenous metoprolol therapy.

### **APPROVAL & LABELING**

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.

### **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 FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible via publicly available labeling repositories.

### **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 219373.**” Approval of this submission by FDA is not required before the labeling is used.

### **DATING PERIOD**

Based on the stability data submitted to date, the expiry dating period for Lopressor (Metoprolol Tartrate) Oral Solution shall be 24 months from the date of manufacture when stored at 20 °C to 25 °C.

### **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 deferring submission of your pediatric study(ies) for ages 0 <18 years of age for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the 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.

- 4804-1 Conduct a study to evaluate efficacy, safety, pharmacokinetics and pharmacodynamics of metoprolol oral solution in pediatric patients 0 to < 18 years old with hypertension.

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<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

Draft Protocol Submission: 05/2025  
Final Protocol Submission: 11/2025  
Study Initiation: 11/2025  
Study Completion: 11/2028  
Final Report Submission: 05/2029

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.<sup>[1]</sup>

Submit the protocol(s) to your IND 163314, with a cross-reference letter to this NDA. Reports of this required pediatric postmarketing study must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from this study. 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.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>3</sup>

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 FDA.gov.<sup>4</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>5</sup>

### **REPORTING REQUIREMENTS**

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

### **POST APPROVAL FEEDBACK MEETING**

New molecular entities qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication

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<sup>3</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

### **COMPENDIAL STANDARDS**

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website<sup>6</sup>.

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

Sincerely,

*{See appended electronic signature page}*

Mary Ross Southworth, PharmD  
Deputy Director for Safety  
Division of Cardiology and Nephrology  
Office of Cardiology, Hematology,  
Endocrinology and Nephrology  
Office of New Drugs  
Center for Drug Evaluation and  
Research

#### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Instructions for Use
- Carton and Container Labeling

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<sup>6</sup> <https://www.uspnf.com/>

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**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.**  
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/s/  
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MARY R SOUTHWORTH  
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