CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

214439Orig1s000

Trade Name:	NORLIQVA oral solution
Generic or Proper Name:	Amlodipine
Sponsor:	CMP Development LLC
Approval Date:	February 24, 2022
Indication:	NORLIQVA oral solution is indicated for the treatment of hypertension in adults and children 6 years and older, to lower blood pressure, and coronary artery disease [Chronic Stable Angina, Vasospastic Angina (Prinzmetal's or Variant Angina) and Angiographically Documented Coronary Artery Disease in patients without heart failure or an ejection fraction <40%].

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214439Orig1s000

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APPROVAL LETTER

NDA 214439

NDA APPROVAL

CMP Development LLC
Attention: Ellen Chrismon
Regulatory Affairs Director
P.O. Box 147
8026 US Highway 264A
Farmville, NC 27828

Dear Ms. Chrismon:

Please refer to your new drug application (NDA) dated and received June 22, 2020, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Norliqva (amlodipine) oral solution.

We acknowledge receipt of your amendment dated August 25, 2021, which constituted a complete response to our April 22, 2021, action letter.

This NDA provides for the use of Norliqva (amlodipine) oral solution for the treatment of:

- Hypertension in adults and children 6 years and older, to lower blood pressure.
- Coronary artery disease [Chronic Stable Angina, Vasospastic Angina (Prinzmetal's or Variant Angina) and Angiographically Documented Coronary Artery Disease in patients without heart failure or an ejection fraction <40%.]

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information) as well as annual reportable changes not included in the

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

enclosed labeling. 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.*[2]

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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 214439**." 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 Norliqva (amlodipine) 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 waiving the pediatric study requirements for age birth to 16 years for the treatment of coronary artery disease because studies are impossible or highly impracticable.

We are deferring submission of your pediatric studies in hypertensive pediatric patients age birth to less than 6 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and

[2] 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.

section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

4239-1 Conduct a dose-ranging juvenile toxicology and toxicokinetic study to support the definitive toxicology study, and conduct a toxicity study in juvenile rats to evaluate developmental toxicity, including potential effects on reproductive development and learning. The study protocol should be agreed with the FDA prior to initiation of the study.

Final Protocol Submission:	09 /2022
Study Completion:	08 /2023
Final Report Submission:	01 /2024

4239-2 Conduct an open-label, randomized, single oral dose, two-treatment, two-period, two-sequence crossover bioequivalence and bioavailability study of amlodipine (ethanol-containing) oral solution versus amlodipine (ethanol-free) oral solution in healthy adults under fasting conditions.

Final Protocol Submission:	09 /2022
Study/Trial Completion:	08 /2023
Final Report Submission:	11 /2023

4239-3 Conduct a dose-ranging, safety, tolerability, and efficacy study of amlodipine besylate oral solution for the treatment of hypertension in pediatric patients birth to <6 years of age. The study protocol should be agreed with the FDA prior to initiation of the study.

Final Protocol Submission:	10 /2024
Study/Trial Completion:	08 /2028
Final Report Submission:	02 /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.[3]

Submit the protocols to your IND 141056, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies 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 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.

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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.*[4]

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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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 contact Sabry Soukehal, Regulatory Health Project Manager, at (240) 402 6187.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, MD, PhD
Director
Division of Cardiology and Nephrology
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
- Container Labeling

[4] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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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.

/s/

NORMAN L STOCKBRIDGE
02/24/2022 02:26:46 PM