OFFICE OF CARDIOLOGY, HEMATOLOGY, ENDOCRINOLOGY, AND NEPHROLOGY
DIVISION OF CARDIOLOGY AND NEPHROLOGY

DIVISION OF REGULATORY OPERATIONS FOR CARDIOLOGY, HEMATOLOGY, ENDOCRINOLOGY, AND NEPHROLOGY

Prior Approval Supplement Review

I. GENERAL INFORMATION

NDA: 214439

Supplement No.: 001

Drug: Norliqva (amlodipine oral solution 1 mg/mL)

Drug class: Calcium channel blocker

Applicant: CMP Development LLC.

Approved indications: Norliqva is indicated 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%.]

II. REVIEW TEAM

Office of Cardiology, Hematology, Endocrinology, and Nephrology (OCHEN) – Division of Cardiology and Nephrology (DCN)

Deputy Director for Safety: Selena DeConti
Associate Director for Labeling: Michael Monteleone
Pediatric Medical Officer: Kirtida Mistry
Regulatory Project Manager for Safety: Lori Wachter

OCHEN – Division of Pharmacology and Toxicology - Cardiology, Hematology, Endocrinology, and Nephrology

Reviewer: Phillip Gatti
Team Leader: Xuan Chi

Office of Clinical Pharmacology – Division of Cardiometabolic and Endocrine Pharmacology

Primary reviewers: Leslie Kenna, Hebing Liu
Secondary reviewer: Brianna Cote

Office of Pharmaceutical Quality

Primary reviewer: Parvin Akther
Secondary reviewer: Joyce Crich
Regulatory Business Project Manager: Grafton Adams

Office of Surveillance and Epidemiology – Division of Medication Error Prevention and Analysis

Primary reviewer: Jody Kundreskas
Team Leader: Nicole Iverson

Office of Regulatory Operations – Division of Regulatory Operations for Cardiology, Hematology, Endocrinology, and Nephrology

Regulatory Health Project Manager: Sabry Soukehal

III. BACKGROUND

Norliqva was approved on February 24, 2022, under the 505(b)(2) pathway for the treatment of hypertension in adults and children 6 years of age and older, and for the treatment of coronary artery disease (chronic stable angina, vasospastic angina, and angiographically documented coronary artery disease in patients without heart failure or an ejection fraction <40%).

To support approval of the NDA, the Applicant submitted reports of bioequivalence studies (19-029 and 19-086) conducted at (b) (4)

At the time of approval, the Agency issued the following postmarketing requirements (PMRs) under the Pediatric Research Equity Act (PREA):

- 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

On February 3, 2023, the Agency released PMR 4239-1 because "another juvenile animal study with amlodipine will not contribute to the assessment of risk for calcium channel blockers for the proposed pediatric trial and is unnecessary."

On February 7, 2024, the Applicant submitted a prior approval supplement (supplement # 001) with a study of an ethanol-free formulation to fulfill PMR 4239-2. The study was conducted at (b) (4)

On June 10, 2024, DCN was notified of a data integrity issue at (b) (4) the lab that conducted the bioequivalence study in support of the original approval of the NDA.

On June 18, 2024, the Applicant was notified of the data integrity issue at (b) (4) and the need to re-conduct their bioequivalence study at a different study site.

On August 8, 2024, the Applicant was notified that a regulatory action cannot be taken on supplement # 001 submitted on February 7, 2024, until resolution of the (b) (4) data integrity issue communicated on June 18, 2024. Although their supplemental NDA 214439/S-001 did not contain data generated by (b) (4) the basis for their supplement was a bioavailability comparison of the reformulated (ethanol-free) drug product to the Norliqva (amlodipine) oral solution, 1 mg/mL approved under NDA 214439.

On June 27, 2025, in response to the June 18, 2024, and August 8, 2024, letters, the Applicant submitted an amendment with the data for the re-conducted bioequivalence study of Amlodipine 1 mg/mL oral solution and Norvasc 10mg tablets, Study C1B05070 performed by (b) (4)

IV. SUPPLEMENT REVIEW

1. Office of Pharmaceutical Quality (OPQ) integrated review: July 22, 2024

Recommendation: Approval

OPQ confirmed that adequate product quality information was provided to support the proposed labeling changes and concluded that the supplement can be approved from a quality perspective.

2. Office of Clinical Pharmacology (OCP) – Division of Cardiometabolic and Endocrine Pharmacology: July 24, 2024, and January 22, 2026

Recommendation: PREA PMR fulfillment

July 24, 2024: OCP reviewed the results of study C1B02037 titled "Single dose oral bioequivalence study of Amlodipine Oral Solution, 1 mg /mL and Norliqva (Amlodipine) Oral Solution, 1 mg/mL in healthy adult human subjects under fasting conditions". The study was designed to evaluate bioequivalence between the ethanol-containing and

ethanol-free formulations. OCP concluded that the study results support fulfillment of PREA PMR 4239-2.

January 22, 2026: OCP reviewed the results of study C1B05070 titled “Single dose oral bioequivalence study of Amlodipine 1mg/mL Oral Solution (Dose = 10mg/10mL) and Norvasc (amlodipine besylate) 10 mg tablets in healthy adult human subjects under fasting conditions”. The primary objective of the study was to compare and evaluate the oral bioavailability of amlodipine oral solution, 1 mg/mL with that of Norvasc (amlodipine besylate) 10 mg tablets in healthy adults under fasting conditions.
OCP concluded that the Applicant conducted the study in accordance with the Product Specific Guidance for Amlodipine besylate and that the Applicant has established pharmacokinetic similarity between their new formulation and the reference.

3. Labeling reviews

Office of Surveillance and Epidemiology – Division of Medication Error Prevention and Analysis (DMEPA) – July 26, 2024, August 6, 2024, and January 27, 2026

DMEPA reviewed the proposed prescribing information and container label to identify areas of vulnerability that could lead to medication errors. They identified areas where the label may be improved to promote the safe use of the product. Comments were sent to the Applicant, and a final agreed-upon labeling was reached on January 27, 2026.

4. Pediatric Review

The fulfillment of PREA PMR 4239-2 was discussed with the Pediatric review committee (PeRC) on January 27, 2026. The PeRC agreed with the Division’s assessment that this PMR was fulfilled.

V. CONCLUSION

The Division of Cardiology and Nephrology recommends approving this supplement. The Division also concludes that the requirement for PREA PMR 4239-2 is fulfilled.

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/s/

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