Cross-Discipline Team Leader and Division Summary Review

Date	7/22/25
From	Elly Moon
Through	Aliza Thompson
Subject	Cross-Discipline Team Leader and Division Summary Review
NDA/BLA # and Supplement #	NDA 219531
Applicant	Brillian Pharma Inc.
Date of submission	7/19/2024
Date of receipt	9/24/2024
PDUFA Goal Date	7/24/2025
Proprietary Name	SDamlo
Established or Proper Name	Amlodipine
Dosage form(s)	Powder for oral solution
Applicant Proposed Indication(s)/ Population(s)	• For the treatment of hypertension, to lower blood pressure in adults and pediatric patients 6 years of age and older • For the symptomatic treatment of chronic stable angina in adults • For the treatment of confirmed or suspected vasospastic angina in adults • In adult patients with recently documented coronary artery disease by angiography and without heart failure or an ejection fraction <40%, to reduce the risk of hospitalization for angina and to reduce the risk of a coronary revascularization procedure
Applicant Proposed Dosing Regimen(s)	Adult: 5 to 10 mg once daily Pediatric: 2.5 mg to 5 mg once daily
Recommendation on Regulatory Action	*Approval*
Recommended Indication(s)/ Population(s) (if applicable)	See "Applicant Proposed Indication(s)/ Population(s)"
Recommended Dosing Regimen(s) (if applicable)	See "Applicant Proposed Dosing Regimen(s)"

Material Reviewed/Consulted	
Integrated Quality Review (7/10/2025)	Stephanie Springer, George Ward, Zhongqiang (Jacky) Lin, Min Sung Suh, Aditi Das, Zhengfu Wang, Feiyan Jin, Haritha Mandula, Yuansha Chen, Esther Jones, Theodore Carver
Pharmacology-Toxicology Review	Not applicable
Clinical Pharmacology Review (7/14/2025)	Ritika Kurian, Elly Moon
Clinical Review	Not applicable
Office of Prescription Drug Promotion Reviews (OPDP) and Division of Medical Policy Programs (DMPP) (6/25/2025)	Laurie Buonaccorsi, Meena Savani, Barbara Fuller
Division of Medication Error Prevention and Analysis (DMEPA) Review (6/2/2025, 7/14/2025, and 7/22/2025)	Christina Topper, Nicole Iverson, and Hina Mehta

1. Introduction

On July 19, 2024, Brillian Pharma, Inc. submitted NDA 219531 for Sdamlo (amlodipine powder for oral solution, 2.5 mg, 5 mg, and 10 mg) pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act.[1] The Applicant is seeking the same indications as the listed drug (LD), Norvasc (amlodipine) tablets (NDA 019787). The application primarily relies on the Agency's previous finding of safety and effectiveness for Norvasc tablets. The NDA is supported by a pivotal relative bioavailability (BA) and food effect study (Study ARL/22/073) comparing Sdamlo oral solution, 5 mg and Norvasc oral tablets, 5 mg.

2. Background

Amlodipine is a calcium channel blocker that is approved for use alone or in combination with other antihypertensive agents and antianginal agents for the treatment of hypertension and coronary artery disease. The Applicant has developed an oral solution formulation of amlodipine. The Applicant claims that their formulation is designed to improve upon unmet needs of the current marketed oral solid and liquid products by providing an age-appropriate dose form that does not require cold chain storage

[1] Because the Applicant had not submitted the proper user fee documentation, the Agency notified the Applicant on July 31, 2024, that the application was not acceptable for filing. On September 24, 2024, the Agency notified the Applicant that their request for a small business user fee waiver, submitted on March 5, 2024, was granted. As a result, the marketing application was considered received on September 24, 2024, and was then filed on November 23, 2024.

conditions. The Applicant proposes to use the same dosing regimen as in the prescribing information for the LD.

3. Product Quality

The Office of Pharmaceutical Quality recommends approval. Their summary review states the following.

Drug Substance: The drug substance information is cross-referenced to DMF (b) (4). The DMF was found to be adequate to support this NDA.

Drug Product: The drug product is a freeze-dried powder that is mixed with water (provided separately) to yield a solution for oral use. The excipients are compendial and present in acceptable amounts. (b) (4) (b) (4) (b) (4) The 24-month shelf-life at 20-25 °C is supported by long term (24 months), intermediate (12 month) and accelerated (6 months) stability data for the three strengths.

Manufacturing:
Process – The manufacturing process includes (b) (4) freeze-drying, (b) (4). The manufacturing process and control are considered acceptable.
Facilities – The drug substance facility was determined to be acceptable based on previous inspection histories. The drug product facility was evaluated through remote regulatory assessment and was considered adequate.

Biopharmaceutics: The biopharmaceutics review assessed biowaiver requests for two strengths (2.5 mg and 10 mg) of the drug product. The provided in vitro data (dissolution and physicochemical property comparison) and proportional similarity of the formulation support the biowaiver request for the 2 strengths. Therefore, the reviewer recommends that the biowaiver request be granted.

Microbiology: According to the microbiology review, the batch release and stability test methods and other microbiological information provided are adequate to support product quality.

Quality Labeling: The labeling was determined to be adequate from a quality perspective with edits to address conformance with the salt policy with respect to the active ingredient.

4. Nonclinical Pharmacology/Toxicology

Not applicable. A Nonclinical Pharmacology/Toxicology review was not needed for this NDA.

5. Clinical Pharmacology

The Office of Clinical Pharmacology recommends approval of NDA 219531. The NDA is primarily supported by a relative bioavailability study, ARL/22/073, which was a single dose three way cross-over study comparing the relative bioavailability (BA) and the effect of food on Sdamlo oral solution and Norvasc tablets in healthy volunteers.

Study ARL/22/073 showed that following administration of 5 mg amlodipine under fasting conditions, the C_{max} and AUCs for both products were comparable (the test/reference geometric mean ratios (GMR) and 90% confidence intervals (CI) were 0.93 (0.88-0.98) and 0.91 (0.86-0.96) for C_{max} and $AUC_{0\text{-}inf}$, respectively). Therefore, a scientific bridge was established between Sdamlo oral solution and the LD, Norvasc tablets.

Administration of Sdamlo under fed conditions (high-fat, high-calorie meal) did not have any impact on the rate or extent of absorption compared to fasting conditions (GMR and 90% CI were 0.98 (0.91-1.01) and 0.94 (0.94-1.06) for C_{max} and $AUC_{0\text{-}inf}$, respectively). The lack of food effect is consistent with the food effect reported in the labeling for LD. Therefore, the product can be approved with the same dosage and administration recommendations as the LD.

6. Clinical Microbiology

Not applicable.

7. Clinical/Statistical-Efficacy

The application relies on the Agency's previous finding of effectiveness for the LD, based on the establishment of a PK bridge between Sdamlo oral solution and Norvasc oral tablets as described under Clinical Pharmacology.

8. Safety

The application relies on the Agency's previous finding of safety for the LD. There were no concerning safety findings in study ARL/22/073.

9. Advisory Committee Meeting

The application does not raise significant issues regarding the safety or effectiveness of the drug; hence, no Advisory Committee Meeting was held or needed.

10. Pediatrics

This application triggers the Pediatric Research Equity Act (PREA) because it is a new dosage form for amlodipine. There is an agreed-upon initial pediatric study plan (iPSP) under IND 157136 (dated February 21, 2024) which includes a plan for a deferral of clinical studies for hypertension in pediatric patients ranging from 0 to <6 years old and a full waiver of clinical studies for coronary artery disease (CAD) in pediatric patients of all ages. As the product is ready for approval, a postmarketing requirement (PMR) for the deferred study in pediatric patients 0 to <6 years old with hypertension will be requested (see Section 14).

11. Other Relevant Regulatory Issues

None.

12. Labeling

The Office of Prescription Drug Promotion (OPDP) and Division of Medical Policy Programs (DMPP) reviewed prescribing information (PI), carton and container labeling, and instruction for use (IFU) and provided comments on the proposed product labeling.

The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) reviewed PI, patient package insert (PPI), IFU, and carton and container labeling and consider these acceptable.

13. Recommended Regulatory Action

The reviews from each discipline recommend approval. We concur that the application can be approved.

14. Postmarketing Requirement

The following PMR, agreed upon with the Pediatric Review Committee and the Applicant, will be issued at the time of approval:

Conduct a dose-ranging, safety, tolerability, and efficacy study of amlodipine 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 (PMR # 4873-1).

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/

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