CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219531Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number.	219531		
Applicant Name	Brillian Pharma, Inc.		
Drug Product Name	SDAMIO (amlodipine)		
Dosage Form.	For solution		
Proposed Strength(s)	2.5 mg, 5 mg, and 10 mg		
Route of Administration	Oral		
Maximum Daily Dose	10 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	Hypertension • Sdamlo is indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Coronary Artery Disease • Chronic Stable Angina • Vasospastic Angina (Prinzmetal's or Variant Angina) • Angiographically Documented Coronary Artery Disease in patients without heart failure or an ejection fraction < 40%		
Drug Product Description	Each unit-dose bottle contains 2.5 mg of amlodipine (equivalent to 3.47 mg of amlodipine besylate) in a white to off-white dry powder or powder cake.		
Co-packaged product information	N/A		
Device information:	N/A		
Storage Temperature/ Conditions	20°C to 25°C		
Review Team	**Discipline**	**Primary**	**Secondary**

	Drug Substance	Stephanie Springer	Zhengfu Wang
	Drug Product/ Labeling	George Ward	Theodore Carver
	Manufacturing	Zhongqiang(Jacky) Lin	Feiyan Jin
	Biopharmaceutics	Min Sung Suh	Haritha Mandula
	Microbiology	Aditi Das	Yuansha Chen
	Other (specify):	N/A	
	RBPM	Esther Jones	
	ATL	Theodore Carver	
Consults	N/A		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating:

A shelf life of 24 months is granted for the drug product when stored at 20°C to 25°C.

b. Additional Comments for Action None.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

1) Background

The Applicant, Brillian Pharma, submitted NDA 219531 for Sdamio, (amlodipine) for oral solution, as 2.5 mg, 5 mg, and 10 mg of powder in vials, for treatment of hypertension and coronary artery disease indications. The proposed new dosage form is intended to serve patient populations with difficulty swallowing tablets and capsules. The Applicant

conducted a pivotal relative bioavailability study comparing the proposed drug product to the listed drug, Norvasc® (amlodipine) tablets, 5 mg, the subject of NDA 019787. The review team included all OPQ review disciplines.

2) Drug Substance

The drug substance, amlodipine besylate, is a synthetic small molecule with a single chiral center and is synthesized as a mixture of the R and S enantiomers. The drug substance information is cross-referenced to DMF (b) (4), which has been reviewed and determined to be adequate to support this NDA. The proposed drug substance specification is adequate to support the quality of the drug substance and conforms to the USP monograph for amlodipine besylate. A retest date of (b) (4) is supported by stability data for the drug substance.

3) 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 mannitol and neotame, which are compendial and present in acceptable amounts. (b) (4) (b) (4) (b) (4). The acceptance criteria for impurities in the drug product specification were confirmed to be acceptable in consultation with the nonclinical division. The proposed shelf life of 24 months is supported by 24 months of long term (25C/60%RH), 12 months intermediate (30°C/65%RH), and 6 months accelerated (40°C/75%RH) stability data for three primary drug product batches of each of the three strengths of the drug product. Although the drug substance polymorphic form was found to be stable (b) (4) during long term storage of the drug product, small amounts of (b) (4) were observed in samples stored under accelerated and intermediated storage conditions only. Based on these stability data, a shelf life of 24 months can be granted for the three strengths of the drug product for storage at 20°C to 25°C.

4) Manufacturing

Process – The drug product manufacturing process includes (b) (4) [redacted] After specific risks associated with the drug product and holding times were addressed, (b) (4) [redacted], process controls and equipment descriptions, the process was found to be adequate.

Facilities – The drug substance facility was recommended for approval based on previous inspection history. The drug product facility was evaluated through a Remote regulatory Assessment and found to be adequate. Overall, the manufacturing review recommends approval.

5) Biopharmaceutics

The biopharmaceutics review assessed bridging of formulations clinical development and a biowaiver request for two strengths of the drug product, because the drug product is administered as a solution. The biopharm review concluded that these aspects were adequate and that the biowaiver request could be granted.

6) Microbiology

The microbiology review determined that the batch release and stability test methods and other microbiological information provided in the NDA were adequate to support the drug product quality.

7) Quality Labeling

The labeling will be adequate after final revisions have been made, including conformance with the salt policy with respect to the active ingredient.

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate**
Quality Labeling	**-**	**Adequate**
Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**Adequate**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate

QPA for EA(s): No

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments: None

Comparability Protocols (PACMP): No
Comments: None

Additional Lifecycle Comments:

During pharmaceutical development, the Applicant determined that the aluminum pouch is needed (b) (4) . If the Applicant requests to remove the aluminum pouch as secondary packaging for the drug product, justification should be closely examined (b) (4) .

Theodore Carver

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CHAPTER IV: LABELING

NDA Number	NDA 219531
Assessment Cycle Number	1
Drug Product Name	SDAMLO (amlodipine (b) (4) for Oral Solutions

Assessment Recommendation: Choose an item.

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Adequate	**SD 15**
Patient Information	Adequate	**SD 15**
Instruction for Use (IFU)	Adequate	**SD 15**
Container Labels	Adequate	**SD 8**
Carton Labeling	Adequate	**SD 8**

Brief Description of Outstanding Issues:

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
0007, SD 8	3/7/2025	All Labeling Documents
0015, SD 15	6/5/2025	Updated PI and IFU with 1 tablespoon reconstitution dosing instruction

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

[1] Labeling Review Tool (LRT) (March 2022), including use of consistent terminology for dosage form and unit of measure for strength in the product title and DOSAGE FORMS AND STRENGTHS heading in Highlights, in the DOSAGE AND ADMINISTRATION, DOSAGE FORMS AND STRENGTHS, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING sections (see page 2 of LRT)

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights[2] [21 CFR 201.57(a)(2)]		
Established name(s)[3]	Adequate	Remove (b) (4) from established name and "(b) (4)" from all instances of the established name in the PI.
Route(s) of administration	Adequate	Oral (b) (4)
Controlled drug substance symbol (if applicable)	N/A	
Initial U.S. Approval [§201.57(a)(3)]	Adequate	Initial U.S. Approval: 1992
Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		
Dosage form(s)[4] and strength(s) in metric system[5]	Adequate	Expressed as mg.
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).[6]	Adequate	Salt policy statement added.

[2] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018)

[3] Established name = [Drug] [Route of Administration] [Dosage Form]. Do use not "USP" descriptor in the product title or within the Highlights (see page 3 of LRT).

[4] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018); USP <1151>; USP Nomenclature Guideline

[5] Labeling Review Tool (March 2022, page 13), include limited packaging information; USP <7>

[6] Guidance: *Naming of Drug Products Containing Salt Drug Substances* (June 2015); MAPP 5021.1

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.[8]	N/A	

Assessment: *Adequate*

Adequate once the listed changes above are made.

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		

[7] Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (March 2013)
[8] Guidance: *Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use* (October 2018); USP <659>
[9] See § 201.57(c)(3); draft guidance: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023); Labeling Review Tool (March 2022, page 25)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents and/or soft food[10], storage conditions needed to maintain the stability of the reconstituted or diluted product).	Adequate	Changed to "(b) (4) " from the previous range.
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	Administration instructions are supported by stability and reconstitution data.
For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11]	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and*	N/A	

[10] Draft Guidance: Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments
[11] §201.57(c)(3)(iv)
[12] USP General Notices 2.30 Legal Recognition

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
disposal procedures.x" with x numerical citation to "OSHA Hazardous Drugs."		

Assessment: *Adequate*

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)[13]

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	All three strengths listed.
Strength(s) in metric system	Adequate	All strengths expressed in metric units.
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride). No equivalency statement.	Adequate	(b) (4) included for all three strengths.
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and	Adequate	All three described as a white to off-white dry powder or powder cake.

[13] See § 201.57(c)(4); Labeling Review Tool (March 2022, page 29)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
color and clarity of the solution, when applicable.		
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	

Assessment: *Adequate*

Section 3 is adequate.

1.2.3 Section 11 (DESCRIPTION)[14]

(b) (4)

[redacted]

[14] See § 201.57(c)(12); Labeling Review Tool (March 2022, page 56)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)[15] [§ 201.57(c)(12)(i)(A)].	Adequate	SDAMLO
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	Remove "(b) (4)" from description
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].	Inadequate	Added a salt equivalency statement
List inactive ingredients (not required for oral use, except for colorant) by the USP/NF names in alphabetical order.[16] Avoid brand names. [§ 201.57(c)(12)(i)(C)].	Adequate	Edited to remove only and reformat the description of the inactive ingredients.
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of	N/A	

[15] Use of "USP" descriptor is not required to be included next to the established name throughout Prescribing Information (PI) labeling. If an applicant wants to use the "USP" descriptor next to the established name in the PI, recommend limiting its use to the product quality sections of the Full Prescribing Information (FPI) (i.e., DOSAGE FORMS AND STRENGTHS, DESCRIPTION, HOW SUPPLIED/STORAGE AND HANDLING) (see page 3 of LRT).

[16] Per § 201.100(b)(5)(i) and (ii), flavoring and colorants may be designated as such without naming their components except for FD&C Yellow No 5 and FD&C Yellow No 6, which must be listed per § 201.20. Per § 201.100(b)(5)(iii), trace amounts of harmless substances added solely for individual product identification need not be named. If an applicant wants to use the National Formulary (NF) descriptor next to excipients, recommend limiting its use to the product quality sections of the FPI (see page 3 of LRT). Do not list brand names, e.g., Opadry, Eudragit, Polistirex, etc.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].		
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	Copied from LD label
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	Requested a better structural formula
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	Adequate	White crystalline powder.
For oral prescription drug products, include gluten statement[19] (if applicable).	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity").	Adequate	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

Assessment: *Adequate*

Adequate with the above corrections addressed.

[17] Listed before "indicated for" in INDICATIONS AND USAGE of Highlights section [§ 201.57(a)(6)]; can also search the term "FDA EPC Text Phrases" in FDA's Labeling Resources for Human Prescription Drugs for the most recent EPC list.

[18] Chemical names do not need to be capitalized unless it appears at the beginning of a sentence (see *Preferred IUPAC Names Provisional Recommendation*, September 2004; Chapter 1, par. 16 Name writing, p.80-90).

[19] Draft guidance: *Gluten in Drug Products and Associated Labeling Recommendations* (December 2017)

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)[20]

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s) [§ 201.57(c)(17)].	Adequate	Remove "(b) (4)"
Strength(s) in metric system. [§ 201.57(c)(17)(i)] If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety. No equivalency statement.	Adequate	Strengths listed in metric units and (b) (4) included as well.
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	(b) (4) single use bottle supplied in cartons of 10 bottles.

[20] See § 201.57(c)(17); Labeling Review Tool (March 2022, page 70). Consider including proprietary name and established name.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s) [§ 201.57(c)(17)(iii)].	Adequate	Added color of powder/powder cake.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs." [§ 201.57(c)(17)(iv)]	N/A	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	USP room temperature range stated.
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of	N/A	

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*[21]		
Include information about child-resistant packaging[22] (if chosen by manufacturer).	Adequate	Child resistant cap.

Assessment: *Adequate*

Adequate with the stated changes made.

1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug review division if the product contains any of these inactive ingredients.

Please include your comments about other sections of labeling if they contain product quality information.

[21] Guidance: *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex* (December 2014)
[22] Guidance: *Child-Resistant Packaging Statements in Drug Product Labeling* (August 2019)

1.2.6 Manufacturing Information After Section 17 (for drug products)[23]

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate" or "Inadequate")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer.	Adequate	Add street address and zip code for distributor/manufacturer addresses.

Assessment: *Adequate*

Adequate with the listed changes made.

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information):

IFU Dosing Instructions (SD 15)

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[24]	Adequate	Removed (b) (4) from established name
Special preparation instructions (if applicable).	Adequate	Reconstitution instructions updated to 1 tablespoon.

[23] § 201.1(h)(5) and 201.1(i); Labeling Review Tool (March 2022, page 74)
[24] Established name = [Drug] [Route of Administration] [Dosage Form]

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Storage and handling information (if applicable).	Adequate	Storage conditions listed as USP room temperature range. Storage and handling directions consistent with available stability data.
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differ from the dosage form.	N/A	
Active ingredient(s) (if applicable).	Adequate	
Alphabetical listing of inactive ingredients (if applicable).	Adequate	
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Adequate	Add street address and zip code for manufacturer and distributor

Assessment: *Adequate*

Adequate with the listed changes above.

3.0 CONTAINER AND CARTON LABELING[25]

All three strengths container and carton labels are identical except for the listed strength. Only the 2.5 mg strength labels are replicated below.

3.1 Container Labels[26]

(b) (4)

[redacted]

[25] Carton and Container Labeling Resources

[26] Per § 201.10(h)(2)(i)(1), if the drug container is too small to bear all labeling information required by section 502(e)(1)(A)(ii) and (B) of the FD&C Act, the container label should bear: proprietary name, established name, lot number, the name of the manufacturer, packer, or distributor of the drug.

3.2 Carton Labeling

(b) (4)

[redacted]

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Proprietary name and established name[27], (font size and prominence) [§ 201.10(g)(2)].	Adequate	Yes	SDAMLO (amlodipine (b) (4) for oral solution)

[27] Established name = [Drug] [Route of Administration] [Dosage Form]

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	Adequate	Yes	Strengths expressed in mg.
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	N/A	Yes	Oral use product – not required
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP [§ 201.10(d)(1) & 201.100(b)(4), USP <1121>].	Adequate	Yes	Present.
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	Adequate	No	Carton – contains 10 (b) (4) bottles Container – single dose
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Adequate	Yes	Present
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	Yes	Present
Lot number and expiration date [§ 201.18 & 201.17].	Adequate	Yes	Space marked for it on both labels
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	Yes	USP room temperature range stated for storage conditions.
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms	N/A	Yes	

[28] Express as " XX mg per tablet" or "XX mg per capsule" for strength of professional samples of solid oral dosage form with small net quantities per container (e.g., 5 or less) or blister pack/carton. See Guidance: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)

[29] § 201.51(h): A drug shall be exempt from compliance with the net quantity declaration required by this section if it is an ointment labeled "sample", "physician's sample", or a substantially similar statement and the contents of the package do not exceed 8 grams.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement. (See USP <659>).			
Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5) or limited space per § 201.10(i)(2)].	N/A	Yes	
For parenteral injectable dosage forms, include quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	Yes	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	Yes	
Linear Bar code [§ 201.25(c)(2)].[30]	Adequate	No	Only on carton.
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	No	Only on carton, changed "(b) (4)" to "(b) (4) dosage"
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	No	Only distributor listed on container label. Both on carton label.
"Keep out of reach of children" statement, optional for Rx,	Adequate	No	Only on carton label.

[30] See § 201.25(b)(1)(i) for a list where bar code is not required, e.g., prescription drug samples, medical gases, radiopharmaceuticals, etc.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
required for OTC [§ 201.66(c)(5)(x)].			
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	Adequate	Yes	Add Medication and IFU statement
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	N/A	Yes	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	Yes	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.[31]	N/A	Yes	
And others if space is available.	Adequate	No	Carton label says consume within 60 mins of reconstitution. Container label says consume (b) (4) Directed to harmonize with new IFU.

[31] USP General Notices 3.20 Indicating Conformance

Assessment of Carton Labels and Container Labeling: *Adequate*

Adequate once the recommended changes are made.

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

None with changes described above made.

Primary Labeling Assessor Name and Date: George Ward, Ph.D.

Secondary Assessor Name and Date (and Secondary Summary, as needed): Theodore Carver, Ph.D.

George Ward

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Theodore Carver

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CHAPTER VI: BIOPHARMACEUTICS

For more details about the items in this template, please see Chapter VI (Biopharmaceutics) of the NDA IQA Guide

Product Information	
NDA Number	219531
Assessment Cycle Number	1
Drug Product Name/ Strength	SDAMLO® (Amlodipine) Powder for Oral Solution, 2.5 mg, 5 mg, and 10 mg
Route of Administration	Oral
Applicant Name	Brillian Pharma Inc.
Therapeutic Classification/ OND Division	Division of Cardiology and Nephrology
LD Number	LD: Norvasc® (Amlodipine) Tablet, 5 mg NDA 019787 (Pfizer Laboratories)
Proposed Indication	Treatment of hypertension and coronary artery disease (CADs) in adults and children 6-17 years

Assessment Recommendation: **Adequate**

Assessment Summary:

The Applicant, Brillian Pharma Inc., submitted a 505(b)(2) NDA for approval of SDAMLO® (Amlodipine) Powder for Oral Solution, 2.5 mg, 5 mg, and 10 mg (in a unit-dose container) for the treatment of hypertension and coronary artery disease (CAD) in adults and children 6-17 years. The proposed drug product is relied upon the Listed Drug (LD), Norvasc® (Amlodipine) Tablets, 2.5 mg, 5 mg, and 10 mg approved on 07/31/1992 under NDA 019787, which has an identical active ingredient (amlodipine besylate), route of administration (oral), strengths, dosing regimen, and targeting identical indication as the LD. The only differences between the proposed product and the LD are in formulation composition and dosage form.

The Applicant conducted a pivotal relative bioavailability study to compare the pharmacokinetic parameters of the proposed product (5 mg, powder for oral solution) with the LD (5 mg, tablet) and included a biowaiver request for other strengths, 2.5 mg and 10 mg. This clinical and biowaiver strategies were previously agreed with the Agency via pIND 157136 Written Response Only (WRO) dated 08/18/2021[1], and physicochemical properties of the reconstituted products across the strengths were provided to support the biowaiver request as recommended.

[1] \\CDSESUB1\EVSPROD\nda219531\0000\m1\us\112-other-correspondence\pind-157136-written-responses.pdf

The comparative in vivo (relative bioavailability) study data indicate that the differences in formulation and dosage form between the proposed product and the LD have no significant impact on the drug absorption (Reference is made to Clinical Pharmacology review for additional details). In addition, the provided in vitro (dissolution and physicochemical property comparison) data along with linearity support a biowaiver request for other strengths (2.5 mg and 10 mg). Therefore, the proposed biowaiver request for the two strengths (2.5 mg and 10 mg) is found adequate, and NDA 219531 is recommended for **APPROVAL** of the proposed drug product, SDAMLO® (Amlodipine) Powder Oral Solution, 2.5 mg, 5 mg, and 10 mg, from a Biopharmaceutics perspective.

List of Submissions Being Assessed:

Document(s) Assessed	Date Received
Orig-1 NDA	09/24/2024

Highlight Key Issues from Last Cycle and Their Resolution: None. This is the first review cycle.

Concise Description of Outstanding Issues *(list bullet points with key information and update as needed)*: None

B.1 BCS DESIGNATION

Assessment: *Adequate*
Solubility: High

The solubility data of amlodipine besylate over the physiological pH range was not provided in this submission, but amlodipine is considered as a high solubility drug substance given that amlodipine besylate is known as a BCS Class I drug and the reconstitution time is [redacted] (b) (4) as per the proposed labeling.

Permeability: High
The Applicant did not provide permeability data of amlodipine besylate, instead the absolute bioavailability has been noted in the labeling, stating "Absolute bioavailability has been estimated to be between 64 and 90%" as per the provided literature[2].

Dissolution: See "B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA"

B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA

Assessment: *N/A*

[2] \\CDSESUB1\EVSPROD\nda219531\0000\m5\54-lit-ref\reference-03.pdf

➢ **Drug Product Background**

The proposed drug product is a powder for oral solution that contains 2.5 mg, 5 mg, and 10 mg of amlodipine besylate (drug substance) and the following excipients: mannitol ((b) (4)), neotame (b) (4)). Dissolution testing is not applicable for the proposed product, but the dissolution of the LD, Norvasc® (Amlodipine) 5 mg Tablet was evaluated to demonstrate that the LD exhibits high solubility and rapid dissolution as its dissolution is not the rate-limiting step in drug absorption.

➢ **Dissolution method**

Dissolution testing is not applicable for quality control purpose of the proposed product, instead the Applicant included appearance and reconstitution time tests in the proposed drug product specifications.
A comparative dissolution study was conducted to support high solubility of the amlodipine besylate, and the dissolution method and results are shown in Table 2 and 3.

Table 2. Dissolution method

Apparatus	USP Apparatus 2 (Paddle)
Medium	0.01N HCl
Volume	500 mL
Temperature	37 °C ± 0.5 °C
Speed	75 rpm

Table 3. Comparative dissolution profiles of proposed product and LD

Time (min)	% Released	
	Norvasc Tablet 5 mg (AK5270)	Amlodipine for Oral Solution 5 mg (B-CIB-003)
5		(b) (4)
10		
15		
20		
30		
45		
60		

➢ **Dissolution Acceptance criteria**

Dissolution acceptance criteria are not applicable for the proposed product.

B.3 CLINICAL RELEVANCE OF DISSOLUTION METHOD & ACCEPTANCE CRITERIA *(e.g., IVIVR, IVIVC, In Silico Modeling, small scale in vivo)*

Assessment: *N/A*

Dissolution method and acceptance criteria are not applicable to the proposed amlodipine powder for oral solution.

B.5 MODIFIED RELEASE ORAL DRUG PRODUCTS – *In-Vitro Alcohol Dose Dumping*

Assessment: *N/A*

The proposed drug product is a powder for oral solution where the drug product is completely dissolved in water (reconstitution) prior to administration.

B.11 EXTENDED RELEASE DOSAGE FORMS –*Extended Release Claim*

Assessment: *N/A*

See the details in Section B.5.

B.12 BRIDGING OF FORMULATIONS

Assessment: *Adequate*

The Applicant conducted a pivotal clinical study under fed and fasting conditions to demonstrate bioavailability and bioequivalence of the proposed product (5 mg, powder) to the LD (5 mg, tablet). According to the Applicant, the results indicate that the proposed product is bioequivalent to the LD, and there is no food effect for the proposed product. The Division of Biopharmaceutics defers to Clinical Pharmacology review for detailed evaluation of the clinical study results.

B. 13 BIOWAIVER REQUEST

Assessment: *Adequate*

The Applicant submitted a biowaiver request for the 2.5 mg and 10 mg strengths as agreed upon via Written Response Only (WRO) dated 08/18/2021 under pIND 157136. In the WRO, the Applicant was recommended to provide comparative physicochemical properties (e.g., pH, osmolality) of the proposed drug product after reconstitution across the strengths.

Table 4 and 5 show the formulation proportionality and physicochemical property comparison data to support the biowaiver request.

Table 4. Formulation composition

Component	2.5 mg		5 mg		10 mg	
	Mg/Dose	%	Mg/Dose	%	Mg/Dose	%
Amlodipine Besylate, USP	3.47[1]	(b) (4)	6.94[2]	(b) (4)	13.88[3]	(b) (4)
Mannitol, NF	(b) (4)		(b) (4)		(b) (4)	
Neotame, NF						
						(D) (4)
Total Weight	(b) (4)	100.00%	(b) (4)	100.00%	(b) (4)	100.00%

[1,2,3] Equivalent to 2.5 mg, 5 mg and 10 mg of amlodipine respectively.
(b) (4)

Table 5. Osmolality and pH of 2.5 mg, 5 mg, and 10 mg strengths after reconstitution

Osmolality

2.5 mg

Batch# /Strength	Summary of Osmolarity result (mOsm/kg H2O)			
	Reconstituted with 5 mL water	Reconstituted with 50 mL water	Reconstituted with 100 mL water	Reconstituted with 240 mL water
20220801	72 mOsm/kg	6 mOsm/kg	2 mOsm/kg	0 mOsm/kg
20220802	72mOsm/kg	6mOsm/kg	2mOsm/kg	0mOsm/kg
20220803	71mOsm/kg	6mOsm/kg	3mOsm/kg	0mOsm/kg

5 mg

Batch#	Summary of Osmolarity result (mOsm/kg H2O)			
	Reconstituted with 5 mL water	Reconstituted with 50 mL water	Reconstituted with 100 mL water	Reconstituted with 240 mL water
20220606	143 mOsm/kg	1 mOsm/kg	6 mOsm/kg	1 mOsm/kg
20220701	148 mOsm/kg	16 mOsm/kg	9 mOsm/kg	2 mOsm/kg
20220705	147 mOsm/kg	14 mOsm/kg	8 mOsm/kg	2 mOsm/kg

10 mg

Batch#	Summary of Osmolarity result (mOsm/kg H2O)			
	Reconstituted with 5 mL water	Reconstituted with 50 mL water	Reconstituted with 100 mL water	Reconstituted with 240 mL water
20220804	311 mOsm/kg	27mOsm/kg	12 mOsm/kg	4 mOsm/kg
20220901	285 mOsm/kg	25 mOsm/kg	11 mOsm/kg	2 mOsm/kg
20220902	295 mOsm/kg	24 mOsm/kg	11 mOsm/kg	2 mOsm/kg

pH

Strength	2.5 mg	Batch #		
Testing Items	Acceptance Criteria	20220801	20220802	20220803
pH after reconstitution	Report Results.	5.3	5.5	5.6
Strength	5 mg	Batch #		
Testing Items	Acceptance Criteria	20220606	20220701	20220705
pH after reconstitution	Report Results.	5.4	5.4	5.4
Strength	10 mg	Batch #		
Testing Items	Acceptance Criteria	20220804	20220901	20220902
pH after reconstitution	Report Results.	5.5	5.5	5.4

The results show that the osmolality decreases rapidly as amount of water increases, and the osmolality levels of all strengths are similar when reconstituted with 240 mL water, which is the typical amount water for oral administration.

In addition, the provided literature indicates that osmolality levels of the reconstituted products when administered with additional amount of water are below those found in the gastrointestinal fluid of children (238-248 mOsm/kg, in

population of infants to adolescents)[3], and thus the differences in osmolality among the strengths unlikely have an impact on the drug absorption.
Based on the assessment of the provided data and information, the in vitro comparison data support waiver of in vivo bioavailability studies for the 2.5 mg and 10 mg strengths. Therefore, the proposed biowaiver request is found adequate from a Biopharmaceutics perspective.

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None

Primary Assessor's Name and Date: Min Sung Suh, Ph.D. 05/08/2025

Secondary Assessor's Name and Date: Haritha Mandula, Ph.D. 05/16/2025

[3] Gopal Pawar et.al., Characterisation of fasted state gastric and intestinal fluids collected from children, Eur J Pharm Biopharm. 2021 Jan:158:156-165.

Min Sung Suh

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U.S. FOOD & DRUG ADMINISTRATION

MICROBIOLOGY

Product Information	Indicated for the treatment of Hypertension Coronary Artery Disease (CAD).
NDA Number	219531
Assessment Cycle Number	1
Drug Product Name / Strength	(b) (4)® Amlodipine for Oral Solution/ 2.5 mg, 5 mg, 10 mg
Route of Administration	Oral
Applicant Name	Brillian Pharma Inc.
Manufacturing Site	(b) (4)
Method of Sterilization	NA/ Nonsterile, drug product

Assessment Recommendation: **Adequate**

Theme:

☒ N/A	☐ Depyrogenation Validation Data
☐ Product Sterility Assurance	☐ Product Release and/or Stability Specifications
☐ Media Fill Data	☐ Validation for Product Release and/or Stability Test Method
☐ Validation of Product Test	☐ Other (Requires Division Director Approval)
☐ Due to Consult	

Justification: *view justification statements found at:* **Justification Statements**

N/A

Assessment Summary:

- The submission is **recommended** for approval.

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
Supporting Document # 1	7/19/2024

Supporting Document # 7	2/07/2025

Highlight Key Issues from Last Cycle and Their Resolution:

Concise Description of Outstanding Issues: NA

Supporting Documents: NA

Select Number of Approved Comparability Protocols: 0

S DRUG SUBSTANCE

The drug substance is not sterile; therefore, a quality microbiology review of the drug substance is not necessary.

Assessment:

Adequate

P DRUG PRODUCT
P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

Description of drug product – The proposed product Amlodipine for Oral Solution has three strengths: 2.5 mg, 5 mg & 10 mg. They are freeze-dried powders packaged in unit-dose HDPE bottles with a child resistant cap. The product is reconstituted in the same unit-dose HDPE bottles at the time of administration.

- **Drug product composition -**
(3.2.P.1.)

Component	Amount per unit (mg)			Function	Quality Standard
	2.5 mg	5 mg	10 mg		
Amlodipine Besylate, USP	3.47	6.94	13.88	API	USP + In-house controls
Mannitol, NF	(b) (4)				NF + In-house controls
Neotame, NF					NF + In-house controls
(b) (4)					
Total Weight			(b) (4)	NA	NA

* (b) (4)

Assessment:

Adequate

- **Description of container closure system**
(3.2.P.7.)

The primary CCS is shown in Table below:

CCS component	Description	Manufacturer
Container	(b) (4) Unit-Dose White HDPE Bottle	(b) (4)
Closure	(b) (4) white (b) CRC (Child Resistant Cap) cap with heat induction liner	

Assessment: The applicant provided an adequate description of the drug product composition and container closure system.

Adequate

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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(b) (4)

MICROBIOLOGY LIST OF DEFICIENCIES:

None

Primary Microbiology Assessor Name and Date:
Aditi Das, Ph.D., 3/07/2025

Secondary Assessor Name and Date:
Yuansha Chen, Ph.D., 3/07/2025

Aditi Das

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Yuansha Chen

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