CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215331Orig1s000

PRODUCT QUALITY REVIEW(S)

U.S. FOOD & DRUG ADMINISTRATION

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 215331

Assessment 1

Drug Product Name	Bortezomib Injection
Dosage Form	Injection
Strength	3.5mg/3.5mL and 3.5mg/1.4mL (1 mg/mL and 2.5 mg/mL)
Route of Administration	IV
Rx/OTC Dispensed	Rx
Applicant	MAIA Pharmaceuticals, Inc.
US agent, if applicable	n/a

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original Submission	09/25/2021	All Disciplines
SD-003	12/28/2021	DP
SD-005	03/03/2021	DP, Process

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Rajan Pargani	Haripada Sarker
Drug Product	William Adams	Sherita McLamore
Manufacturing	Caryn McNab	Ephrem Hunde
Microbiology	Jason God	Julie Nemecek
Biopharmaceutics	Anitha Govada	Qi Zhang
Regulatory Business Process Manager	Dahlia Waters	
Application Technical Lead	Sherita McLamore	
Laboratory (OTR)	n/a	n/a
Environmental	n/a	n/a

U.S. FOOD & DRUG ADMINISTRATION

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	Type II		(b) (4)	N/A	12/21/2020	Adequate
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
IND 141660		Development

2. CONSULTS: n/a

Discipline	Status	Recommendation	Date	Assessor

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

Based on the information provided in this application (original submission and amendments in responses to information requests), the OPQ considers all review issues to be adequately addressed and potential risks to patient safety, product efficacy, and product quality mitigated appropriately. Accordingly, OPQ recommends **APPROVAL** of NDA 215331 and grants a **24-month expiration period** for the drug product when protected from light and stored under USP controlled refrigerated conditions (2-8ºC). There are no outstanding issues or post-approval quality agreements to be communicated to the applicant.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

NDA 215331 was submitted as a 505(b)(2) NDA under the Federal Food, Drug and Cosmetic Act. The drug product, Bortezomib Injection 3.5mg/3.5mL and 3.5mg/1.4mL (1 mg/mL and 2.5 mg/mL) is indicated for the treatment of adult patients with multiple myeloma (MM) or mantle cell lymphoma (MCL) (b) (4) Bortezomib is a modified dipeptidyl boronic acid and is a reversible inhibitor of the chymotrypsin-like activity of the 26S proteasome in mammalian cells. Bortezomib was originally approved under the brand name VELCADE® for the treatment of multiple myeloma under NDA 021602 in 2003. VELCADE® is presented as a sterile lyophilized powder in a clear single-use vial that must be reconstituted in either 1.4 mL of 0.9% sodium chloride injection for a nominal concentration of 3.5 mg/1.4 mL (2.5 mg/mL) for subcutaneous (SC) administration or 3.5 mL of 0.9% sodium chloride injection for a nominal concentration of 3.5 mg/3.5 mL (1 mg/mL) for intravenous (IV) administration.

The proposed product, Bortezomib Injection 3.5mg/3.5mL and 3.5mg/1.4mL, is supplied as a refrigerated, ready-to-use (RTU) sterile solution in an (b) (4) single-dose vial. It is available in two presentations: 1 mg/mL and 2.5 mg/mL and is designed for intravenous administration only without the need to reconstitute. The proposed product will differ from the LD only in terms of its dosage form and singular route of administration. The concentration of drug substance in the proposed product is the same as the LD after reconstitution. Additionally, the proposed drug product will have the same indications, route of administration (IV only) and dosing regimen as the reference product.

The recommended starting dose of bortezomib for injection is 1.3 mg/m^2 with a MDD of 1.3 mg/m^2 (1.3 mg/m2* 1.8 = 2.34 mg/day) to be administered without dilution as a 3 to 5 second bolus intravenous injection at a concentration of 1 mg/mL or 2.5 mg/mL. Unlike the LD, t**he proposed product is not intended for subcutaneous administration.**

The bortezomib dosing regimen includes nine- 6-week cycles with dosing weekly (days 1, 4, 8, 11, 22, 25 29 and 32) in cycles 1-4 and once weekly (days 1, 8, 22 and 29) in cycles 5-9.

Proposed Indication(s) including Intended Patient Population	Multiple Myeloma and Mantle Cell Lymphoma	
Duration of Treatment	54 weeks (nine 6-week cycles)	
Maximum Daily Dose	1.3 mg/m^2	
Alternative Methods of Administration	None	

B. Quality Assessment Overview

Drug Substance: Adequate

Bortezomib is a modified dipeptidyl boronic acid proteasome inhibitor that is manufactured as a hydrate. It is a small chiral molecule that is manufactured and release tested (b) (4). The drug substance exists in its cyclic anhydride form as a trimeric boroxine; however, the boroxine is hydrolyzed to the monomeric boronic acid when exposed to an aqueous system.
Bortezomib drug substance is a slightly hygroscopic, white to off white powder that is slightly soluble in water, freely soluble in DMF, DMSO and MeOH and practically insoluble in n-Hexanes. Bortezomib has a very low aqueous solubility and degrades in aqueous media. The drug product is a liquid solution (b) (4) therefore, the polymorphic state of the drug substance is not relevant for MAIA's dosage form.

The applicant references DMF (b) (4) for the manufacture and control of the drug substance. DMF (b) (4) was reviewed in conjunction with this application and was deemed adequate to support the approval of the NDA. Based on the information in the referenced DMF, a (b) (4) retest period has been established for the drug substance by the drug substance manufacturer and NDA 215331 is recommended for approval from a drug substance perspective.

Drug Product: Adequate

Bortezomib Injection is supplied as a refrigerated, ready-to-use, sterile solution in two presentations: 3.5 mg/1.4 mL (2.5 mg/mL) and 3.5 mg/3.5 mL (1 mg/mL). It is a clear, colorless solution packaged in a single-dose vials for intravenous administration only. Each single-dose vial contains the active together with Mannitol USP, Dimethyl Sulfoxide USP, Sodium Acetate USP, Water for Injection USP and Sodium Hydroxide NF/Hydrochloric Acid NF for pH adjustment and does not contain antimicrobial preservatives, novel excipients, or overages.

The 3.5 mg/1.4 mL (2.5 mg/mL) and 3.5 mg/3.5 mL (1 mg/mL) presentations utilize different container closure systems. The 2.5 mg/mL presentation is packaged in 2 mL (b) (4) glass vials with 13-mm neck, stoppered with 13-mm (b) (4) rubber stoppers (b) (4), and sealed with 13-mm aluminum seals with a (b) (4) flip-off cap. The 1 mg/mL presentation is packaged in 5 mL (b) (4) glass vials with 20-mm neck, stoppered with 20-mm (b) (4) rubber stoppers (b) (4), and sealed with a 20-mm aluminum seals with a (b) (4) flip-off cap. The primary container closure system was deemed suitable for the intended use and the rubber closure was demonstrated to be compatible with the drug product based on stability and leachable and extractable studies.

The drug product specification included controls for all critical quality attributes associated with the IV dosage form, comply with compendial standards and are adequate to establish the drug product identity, potency, and purity, and provide adequate controls to ensure the quality of the drug product throughout the product expiry.

In support of the proposed 24-month expiry, 24 months of long-term and 6 months of accelerated primary stability data were provided for three registration batches of the drug product manufactured with the proposed commercial formula, by the proposed commercial process and packaged in the aforementioned container closure system. Based on the available stability data, the applicant proposed, and the OPQ accepts the proposed **24-month** expiration dating period for the drug product when stored at stored under refrigerated conditions (i.e. 2°C and 8°C) and protected from light.

There are no outstanding issues related to the drug product and NDA 215331 is recommended for APPROVAL from a drug product perspective.

Labeling: Adequate

While labeling negotiations are on-going, the proposed labeling and labels include adequate information to meet the regulatory requirements.

Manufacturing: Adequate

The drug product is manufactured and release tested (b) (4) at a commercial batch size of (b) (4) which translates to (b) (4) vials and (b) (4) vials for the 1 mL and 1.4 mL fill volumes, respectively. (b) (4) (b) (4) The manufacturing process ensures the sterility of the final product and the conformity to the release specifications. (b) (4) . The assay and impurities of the drug

substance are impacted by oxidation, heat, light and alkaline pH. Accordingly, the applicant implemented controls during the manufacturing process to mitigate the risks (see appended Process and Facilities review for details). The manufacturing process includes well defined IPCs, CPPs and CQAs and all were described in sufficient detail and were adequately justified. The applicant demonstrated the suitability of the manufacturing process for the drug product at commercial scale. The description of the manufacturing process is comprehensive and includes appropriate in-process controls and operating parameters.

All the DS and DP manufacturing and testing facilities are acceptable based on their previous inspectional history and are acceptable to perform the responsibilities listed in the application. Accordingly, this application is recommended for approval from a manufacturing and facility perspective.

Biopharmaceutics: Adequate

The applicant established a bridge under 21 CFR 320.24(b)(6) between the proposed drug product, Bortezomib Injection, 1 mg/mL and 2.5 mg/mL for intravenous administration and the relied-upon listed drug, Velcade® (bortezomib) 3.5 mg/vial based on the following:

- The proposed drug product is intended for IV administration only
- The proposed drug product contains the same active moiety (bortezomib), route of administration (IV), dosage regimen and indication as that of the LD, Velcade® (bortezomib) 3.5 mg/vial (lyophilized powder, injectable solution upon reconstitution3)
- The Applicant provided a comparison of the physicochemical properties of the proposed Bortezomib for Injection, (b) (4) 1 mg/ml, and the LD, after reconstitution to 1 mg/ml.
- The pH and osmolality of the proposed drug product and the LD (after reconstitution and dilution with 0.9 % sodium chloride injection to 1 mg/mL), are similar for the intravenous route of administration.
- The 2.5 mg/mL strength is compositionally proportional to the 1 mg/mL strength.
- The proposed product has comparable pH (5 vs. 4.7), Osmolality and in vitro hemolytic analysis for tolerability as that of the LD
- The differences in mannitol concentration of the proposed product (b) (4) compared to (2.5%) the LD is justified (b) (4) (b) (4)
- The difference in the composition, i.e. absence of sodium chloride and inclusion of sodium acetate and dimethyl sulfoxide (DMSO) (b) (4) is justified based on the in vitro hemolytic analysis study for demonstration of safety and tolerability similarity
- The administered volumes are slightly different (less than the administrated volume of LD) calculated based on the concentration of active ingredient per mL to follow the same dosage regimen. The dose

administered is based on the body surface are and therefore, the minor difference in volume administration after dilution with 0.9% NaCl is not expected to impact the disposition kinetics of bortezomib.

Therefore, based on the totality of the information provided, the proposed drug product is adequately bridged to the listed drug, under 21 CFR 320.24(b)(6), and an in vivo pharmacokinetic study is not needed. Accordingly, NDA 215331 is recommended for **APPROVAL** from a Biopharmaceutics perspective.

Microbiology (if applicable): Adequate

The microbiology review focused on the sterility assurance of the drug product. The feasibility (b) (4) of the drug product was evaluated to recommend the manufacturing process and it was concluded that Bortezomib (b) (4) Injection is not (b) (4) (b) (4) Adequate information was provided to support the sterility assurance of the drug product for the intended shelf-life.

The validation information supporting the (b) (4) manufacturing demonstrates that the sterilization processes are controlled and are suitable for (b) (4) processing at the drug product manufacturing facilities. Accordingly, NDA 215331 is recommended for approval from a quality microbiology perspective

C. Risk Assessment

From Initial Risk Identification			Assessment		
Attribute/ CQA	**Factors that can impact the CQA**	**Initial Risk Ranking**	**Risk Mitigation Approach**	**Final Risk Evaluation**	**Lifecycle Considerations/ Comments**
Sterility	• Formulation • Container closure • Process parameters • Scale/equipments • Site	H	(b) (4)	Acceptable	N/A
Endotoxin Pyrogen	• Formulation • Container closure	M		Acceptable	N/A

	• Process parameters • Scale/equipments • Site		(b) (4)		
Assay (API), stability	• Formulation • Container closure • Raw materials • Process parameters • Scale/equipments • Site	L		Acceptable	N/A
Uniformity of Dose (Fill Volume/deliverable volume)	• Formulation • Container closure • Process parameters • Scale/equipments • Site	L		Acceptable	N/A
Osmolality	• Formulation • Raw materials • Process parameters • Scale/equipments • Site	L		Acceptable	N/A
pH- (Low)	• Formulation • Container closure • Raw materials • Process parameters • Scale/equipments • Site	L		Acceptable	N/A
Particulate matter (non	• Formulation • Container closure	M		Acceptable	N/A

aggregate for solution only)	• Raw materials • Process parameters • Scale/equipments • Site		(b) (4)		
Leachable extractables	• Formulation • Container closure • Raw materials • Process parameters • Scale/equipments • Site	L		Acceptable	N/A

D. List of Deficiencies for Complete Response

1. Overall Quality Deficiencies *(Deficiencies that affect multiple sub-disciplines)*

n/a

2. Drug Substance Deficiencies

n/a

3. Drug Product Deficiencies

n/a

4. Labeling Deficiencies

n/a

5. Manufacturing Deficiencies

n/a

6. Biopharmaceutics Deficiencies

n/a

7. Microbiology Deficiencies

n/a

8. Other Deficiencies *(Specify discipline, such as Environmental)*

n/a

Application Technical Lead Name and Date:
Sherita D. McLamore *May 26, 2022*

CHAPTER IV: LABELING

Amendments addressed in this review:

SD-001	09/25/21	new NDA
SD-002	10/14/21	label name
SD-003	12/28/21`	updated stability studies
SD-006	03/21/22	vial and carton labels
SD-007	04/15/22	updated USPI

Amendment SD-001

Provided are draft vial labels, carton labels and USPI with comparisons to the Velcade labels and labeling.

Amendment SD-002

The amendment provides revised vial labels, carton labels and USPI in response to comments in an email dated 10/08/21 which recommended that the request for proprietary name review be withdrawn and that the labels and labeling be revised accordingly.

Amendment SD-006

The amendment provides a discussion and a copy of the annotated comparison with the RLD (amendment SD-001) in response to comments in an email dated 03/15/22. The letter expressed a safety concern regarding potential medication errors and the possible used of syringe stickers.

The holder responded that, because MAIA's ready-to-use product does not require reconstitution, it is intended for the practitioner to withdraw the required dose directly from the vial and administer at point of use. Therefore, the proposed drug product does not need to be stored in a syringe prior to administration. The product strength and route of administration are already clearly indicated on the drug product vial. Thus, vial stickers used with Velcade are not needed.

Amendment SD-007

The amendment provides revised USPI in response to FDA editorial comments on the labels and labeling issued in an email dated 04/11/22.

Comment 1: Please refer to your NDA submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Bortezomib Injection. We also refer to your submission dated 09/27/21. Please review the changes/comments and do the following in the same label version provided:

• Accept any changes that you agree with including all format/minor editorial changes
• Edit over the ones that you do not agree with (do not reject any changes that the FDA proposed)
• Please address the comments directly to the document in tracked changes
• Maintain a docx file
• Do NOT anonymize the comments

Response

MAIA agrees with all of FDA's proposed edits and comments, and we have accepted all the proposed changes, including all format/minor editorial changes. We have also addressed the FDA comments directly to the document in tracked changes. In addition, they have revised the storage period for unopened vials at room temperature [redacted] (b) (4) to 7 days in section 2.10 [redacted] (b) (4). The proposed revision is based on the updated stability data provided in amendment SD-003 section 3.2.P.8.3.2 (Short Term Temperature Excursion Study).

1.0 PRESCRIBING INFORMATION – amendment SD-007

Assessment of Product Quality Related Aspects of the Prescribing Information: CMC information is adequate

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Items 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		
Established name(s)[1]	Adequate	Bortezomib injection, for intravenous use
Route(s) of administration	Adequate	3-5 second bolus IV injection
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s)	Adequate	3.5 mg/3.5 mL (1 mg/mL) 3.5 mg/1.4 mL (2.5 mg/mL)
tablet is scored	N/A	
For injectable drug products for parental administration, use appropriate package type term	Adequate	Single dose vials
If the drug product contains an active ingredient that is a salt	N/A	Formulated and dosed as free molecule.

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Items 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		

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

Special instructions for product preparation	Adequate	This is a ready-to-use solution
Important administration instructions	N/A	
For parenteral products: include statement: *"Parenteral drug products must be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit"*	Adequate	Statement is present
If there is a USP monograph for the drug product	N/A	Th draft Pharmacopeia Forum monograph is referenced.
For radioactive products,	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]"* with x numerical citation to "OSHA Hazardous Drugs".	Adequate	Drug is cytotoxic.

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Items 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	Solution for (b) (4) injection
Strength(s) in metric system	Adequate	1.0 mg/mL and 2.5 mg/mL
If the active ingredient is a salt,	Adequate	Formulated and dosed as the free molecule.
A description of the identifying characteristics of the dosage forms,	Adequate	Clear colorless solution
If the tablet is scored.	N/A	
For injectable drug products for parental administration, use appropriate package type.	Adequate	Single dose (b) (4) glass vial

Section 11 (DESCRIPTION)

Item	Items 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)	Adequate	Bortezomib Injection, for intravenous use
Dosage form(s) and route(s) of administration	Adequate	Ready-to-use solution for (b) (4) IV injection
If the active ingredient is a salt,	N/A	
List names of all inactive ingredients.	N/A	
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.	Adequate	• 1 mg/mL: each mL contains 1 mg bortezomib, 10 mg mannitol USP, 0.82 mg sodium acetate USP, 20 mg dimethyl sulfoxide USP in water for injection USP; pH adjusted with HCl NF or NaOH NF • 2.5 mg/mL: each mL contains 2.5 mg bortezomib, 25 mg mannitol USP, 0.82 mg sodium acetate USP, 22 mg dimethyl sulfoxide USP in water for injection USP; pH adjusted with HCl NF or NaOH NF
If alcohol is present	N/A	
Sterility statement (if applicable)	Adequate	present
Pharmacological/Therapeutic class	Adequate	proteasome inhibitor
Chemical name, structural formula, molecular weight	Adequate	Information is complete and correct
If radioactive	N/A	
Other important chemical or physical properties (such as pKa or pH)	Adequate	Aqueous solubility

Section 11 (DESCRIPTION) Continued

Item	Items 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)
For oral prescription drug products	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity") None are present	Adequate	(b) (4) is deleted from established name during label discussion
If there is a USP monograph for the drug product	N/A	Draft PF monograph is referenced

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Items 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)	Adequate	a ready-to-use, sterile solution, individually cartoned vials
Strength(s) in metric system	Adequate	1.0 mg/mL and 2.5 mg/mL
Available units (e.g., bottles of 100 tablets)	Adequate	3.5 mg/3.5 mL (1mg/mL) in a 5 mL vial 3.5 mg/1.4 mL (2.5 mg/mL) in a 2 mL vial
Identification of dosage forms)	Adequate	solution
If the tablet is scored.	N/A	
For injectable drug products for parental administration, use appropriate package type term	Adequate	Single dose vials
Special handling about the supplied product to "OSHA Hazardous Drugs." And light protection	Adequate	Follow guidelines for handling and disposal for hazardous drugs, including the use of gloves and other protective clothing to prevent skin contact. Store in the original package to protect from light.

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Items in Proposed Labeling	Assessor's Comments

	(choose "Adequate", "Inadequate", or "N/A")	(If an item is Inadequate, provide more details on the issues, as appropriate)
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Adequate	Store Bortezomib Injection in a refrigerator at 2° to 8°C (36° to 46°F) in the original package to protect from light.
Latex"	N/A	
Include information about child-resistant packaging	N/A	

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.

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Items 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)
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	Distributed and Marketed by: MAIA Pharmaceuticals, Inc. 707 State Road, Suite 104 Princeton, NJ 08540 Made in India

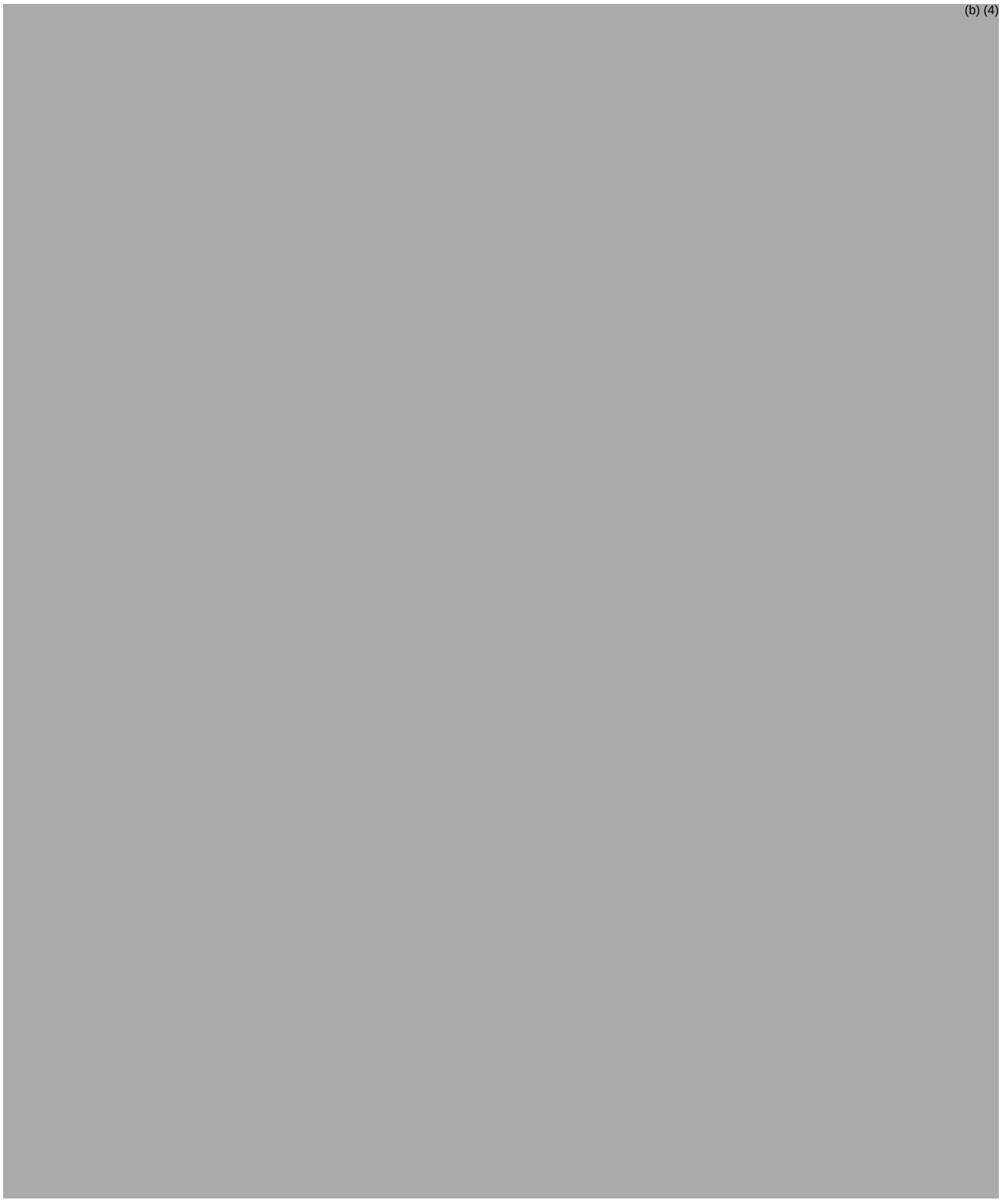
2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information): None

Any deficiencies should be listed at the end in the "ITEMS FOR ADDITIONAL ASSESSMENT." None

3.0 CONTAINER AND CARTON LABELING

(b) (4)



1 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[2], (font size and prominence)	Adequate	Present and correct
Strength(s) in metric system	Adequate	Present and correct
Route(s) of administration	Adequate	Present and correct
If the active ingredient is a salt,	N/A	
Net contents (e.g., tablet count, volume of liquid)	Adequate	3.5 mg per 3.5 mL (1 mg/mL) 3.5 mg per 1.4 mL (2.5 mg/mL)
"Rx only" displayed on the principal display	Adequate	Present
NDC	Adequate	Present
Lot number and expiration date	Adequate	Present
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Adequate	Storage statement is present. No BUD
For injectable drug products for parental administration, use appropriate package type term	Adequate	Single dose vial
For parenteral injectable dosage forms, include the name and quantities of all active and inactive ingredients in alphabetical order. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	Adequate	Present and complete
If alcohol is present	N/A	
Linear Bar code	Adequate	Present

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

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Name of manufacturer/distributor /packer	Adequate	Present and correct
If there is a Medication Guide	N/A	
No text on Ferrule and Cap overseal, unless a cautionary statement is required.	Adequate	(b) (4) .
If there is a USP monograph	N/A	
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.	N/A	
And others, if space is available.	N/A	

Assessment of Carton and Container Labeling: ***{Adequate}***

Any deficiencies should be listed at the end in the "ITEMS FOR ADDITIONAL ASSESSMENT.": None

ITEMS FOR ADDITIONAL ASSESSMENT

None

Overall Assessment and Recommendation:

Acceptable

Primary Labeling Assessor Name and Date:

William Adams, CMC-DP Reviewer/ONDP 05/16/22

Secondary Assessor Name and Date (and Secondary Summary, as needed):

Sherita McLamore, SPQA, ONDP *mm/dd/22*

William Adams

Digitally signed by William Adams
Date: 5/16/2022 03:34:29PM
GUID: 508da7220002a12c3e992e212029c42b

Sherita McLamore

Digitally signed by Sherita McLamore
Date: 5/18/2022 08:36:37AM
GUID: 5032579500004157554 92db5bb8b1a5c

BIOPHARMACEUTICS REVIEW for NDA SUBMISSIONS	
Application No.	NDA 215331-ORIG-1
Type of Submission	505(b)(2)
Applicant/Sponsor	MAIA Pharmaceuticals, Inc.
Product Name	Bortezomib for Injection [redacted] (b) (4)
Dosage Form/Strength	1 mg/mL and 2.5 mg/mL (Supplied in two presentations – 3.5 mg/3.5 mL (1 mg/mL) and 3.5 mg/1.4 mL (2.5 mg/mL)
Route of Administration	Injectable /Intravenous (IV)
Intended Use	Bortezomib Injection is a is a modified dipeptidyl boronic acid1 that functions as a proteasome inhibitor indicated for treatment of adult patients with multiple myeloma and adult patients with mantle cell lymphoma.
Submission Date	9/24/2021[1] (Original Submission)
Recommendation	**Adequate**

EXECUTIVE SUMMARY:

The proposed drug product, Bortezomib for Injection, 1 mg/mL (i.e. 3.5 mg/3.5 mL) and 2.5 mg/mL (i.e. 3.5 mg/1.4 mL), is a ready to use (RTU) solution[2], for intravenous (IV) administration. The proposed drug product has the same active ingredient (bortezomib), same indication, route of administration and dosage regimen as the Listed Drug, Velcade® (bortezomib) 3.5 mg/vial (which may be reconstituted to either 1 mg/mL for intravenous or subcutaneous and 2.5 mg/mL for subcutaneous.) The proposed drug product is different from the LD in terms of dosage form (ready to use sterile solution vs lyophilized powder for reconstitution), strengths (addition of 2.5 mg/mL), and formulation compositions [(b) (4) inclusion of sodium acetate and dimethyl sulfoxide (DMSO) (b) (4)].

The applicant established a bridge under 21 CFR 320.24(b)(6) between the proposed drug product, Bortezomib Injection, 1 mg/mL and 2.5 mg/mL for intravenous administration and the relied-upon listed drug, Velcade® (bortezomib) 3.5 mg/vial based on the following:

- The proposed drug product is intended for intravenous administration only

[1] \\CDSESUB1\evsprod\nda215331\0001\m1\us\12-cover-letters\cover-letter-0001.pdf

[2] The proposed Bortezomib (b) (4) Injection is a ready to administer parenteral solution and simulates the LD in strengths after reconstitution but is indicated for intravenous use only.

- *The proposed drug product contains the same active moiety (bortezomib), route of administration (IV), dosage regimen and indication as that of the LD, Velcade® (bortezomib) 3.5 mg/vial (lyophilized powder, injectable solution upon reconstitution[3])*
- The Applicant provided a comparison of the physicochemical properties of the proposed Bortezomib for Injection, after dilution to 1 mg/ml, and the LD, after reconstitution to 1 mg/ml.
- The pH and osmolality of the proposed drug product and the LD (after reconstitution and dilution with 0.9 % sodium chloride injection to 1 mg/mL), are similar for the intravenous route of administration.
- The 2.5 mg/mL strength is compositionally proportional to the 1 mg/mL strength.
- The proposed product has comparable pH (b) (4), Osmolality and in vitro hemolytic analysis for tolerability as that of the LD
- The differences in mannitol concentration of the proposed product (b) (4) compared to (2.5%) the LD is justified (b) (4) (b) (4)
- The difference in the composition, (b) (4) inclusion of sodium acetate and dimethyl sulfoxide (DMSO) (b) (4) is justified based on the in vitro hemolytic analysis study for demonstration of safety and tolerability similarity
- The administered volumes are slightly different (less than the administrated volume of LD) calculated based on the concentration of active ingredient per mL to follow the same dosage regimen. The dose administered is based on the body surface are and therefore, the minor difference in volume administration after dilution with 0.9% NaCl is not expected to impact the disposition kinetics of bortezomib.

Therefore, the disposition kinetics of Bortezomib should be similar from the proposed [MAIA's Bortezomib Injection, 2.5 mg/mL (3.5 mg in 1.4 mL vial and 2.5 mg in 1 mL vial)] and the LD product, Velcade® (bortezomib) 3.5 mg/vial].

Based on the totality of the information provided, the proposed drug product is adequately bridged to the listed drug, under 21 CFR 320.24(b)(6), and an in vivo pharmacokinetic study is not needed for the proposed route of administration only.

From the Biopharmaceutics perspective, NDA 215331 for Bortezomib for Injection, 2.5 mg/mL (i.e., 3.5 mg/1.4 mL) and 1 mg/mL (i.e., 3.5 mg in 3.5 mL) presentations is recommended for **APPROVAL** for intravenous route of administration.

[3] https://www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/1121Nomenclature.pdf

SUBMISSION:

MAIA Pharmaceuticals Inc. submitted the current NDA for Bortezomib (b) (4) solution for Injection, 2.5 mg/ml and 1 mg/mL for IV use under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. The Applicant acknowledges that its proposed product does not satisfy the waiver of evidence of in vivo bioavailability under 21 CFR 320.22(b)(l), because it does not contain the same inactive ingredients in the same concentrations as the Listed Drug (LD).

The 505 (b)(2) application relies on FDA's findings of safety and effectiveness for the listed drug (LD), Velcade® (bortezomib) for Injection lyophilized powder for injection, 3.5 mg/vial [for intravenous and subcutaneous administration] marketed by Millennium Pharmaceuticals under the approved NDA 021602. As discussed in the pre-NDA meeting, the sponsor submitted the bridging report to establish bridge between the proposed and LD products as per 21 CFR 320.24(b)(6). To support the bridging of the additional strength 2.5 mg/mL for intravenous administration, including justification with supporting data, (side by side comparison of formulations (1 mg/mL and 2.5 mg/mL of the proposed product and the LD) and physicochemical characterization [pH, tonicity, osmolality, drug concentration, administered volume and comparative in vitro hemolysis study results] demonstrating that the differences between the proposed injectable (liquid dosage form as ready to use solution) and LD product (lyophilized powder for solution), do not have any impact on the disposition, efficacy and safety of the proposed drug product

BIOPHARMACEUTICS REVIEW:

The LD, NDA 021602 for Velcade® (bortezomib) for Injection, is lyophilized powder supplied as 3.5 mg of bortezomib as a white to off-white cake or powder per vials. The LD, as specified in the Velcade® product label, must be reconstituted with 3.5 mL of 0.9% w/v sodium chloride to a concentration of 1 mg/mL, for injection prior to the IV administration and 1.4 mL of 0.9% w/v sodium chloride (2.5 mg/mL) for the subcutaneous injection.

MAIA developed a ready to use (RTU) liquid dosage form of Bortezomib for Injection, a 2.5 mg/ml and 1 mg/mL solution, which is intended to be used without further dilution for the same indication, same route of administration[4], and same dosing regimen as the LD, Velcade® (bortezomib) for injection.

MAIA's 2.5 mg/mL strength is supplied as 1.4 mL/**vial** and 1 mg/mL strength is supplied as 3.5 mL/**vial** for IV administration. The proposed concentration 1 mg/mL is identical to the concentration for IV administration of the LD, Velcade® (bortezomib) for injection, 3.5 mg/vial after reconstitution to 1mg/mL). Applicant states that because the dosage regimen (1.3 mg/m^2 dose) is same as the LD Velcade, the proposed concentrations of 1 mg/mL and 2.5 mg/mL does not pose any safety or efficacy concerns.

[4] Note: This review is focused on the intravenous administration of proposed product. (b) (4)

The concentration of active ingredient [redacted] (b) (4) from the proposed 3.5 mg/vial product remains the same as the 3.5 mg/vial presentation of the LD product for IV administration. The proposed drug product, Bortezomib [redacted] (b) (4) Injection is formulated with mannitol, dimethyl sulfoxide, sodium acetate, and sodium hydroxide and/or hydrochloric acid. As recommended in the Pre-NDA meeting (July 29, 2021)[5], for the establishment of a scientific bridge between the LD and the proposed formulation which differ in inactive ingredients, the Applicant submitted in vitro comparative physicochemical data, data from in vitro hemolysis experiment to demonstrate tolerability, and published literature data to demonstrate that the difference in the excipients do not affect the disposition kinetics of bortezomib in human subjects.

1. A physicochemical comparison of MAIA's Bortezomib [redacted] (b) (4) Injection 1 mg/mL and 2.5 mg/mL compared to the LD is provided in the table below.

Bortezomib [redacted] (b) (4) Injection 1 mg/mL is comparable to the LD in terms of the comparative in vitro physicochemical data, such as pH and osmolality, and the volume of drug product administered is identical to the LD (2.34 mL for a 1.8 m^2 BSA patient). Table 1 provides a side-by-side comparison, demonstrating that the conditions of use, active ingredient, route of administration, final dosage form, total volume of administration, strengths of the proposed drug product are similar to those of the LD.

[5] \\CDSESUB1\evsprod\nda215331\0001\m1\us\112-other-correspondence\pre-nda-meeting-minutes-ref-id-4833651.pdf

Table 1a: Comparison of the proposed product Bortezomib Injection 1 mg/mL, with the LD VELCADE® 3.5mg/vial

Component	MAIA 1 mg/mL [3.5 mL/vial] Bortezomib for Injection	MAIA 2.5 mg/mL [1.4 mL/vial] Bortezomib for Injection	VELCADE® (bortezomib) 3.5 mg/vial for Injection	Function
	Quantity per Milliliter (mL)	Quantity per Milliliter (mL)	Quantity per Milliliter (mL)	
Route of Administration	IV	IV	IV, SC	
Indication	Treatment of adult patients with multiple myeloma and for treatment of adult patients with mantle cell lymphoma	Treatment of adult patients with multiple myeloma and for treatment of adult patients with mantle cell lymphoma	Treatment of adult patients with multiple myeloma and for treatment of adult patients with mantle cell lymphoma	
Dosage Form	Ready to Use Solution for Injection	Ready to Use Solution for Injection	Lyophilized Powder for Injection upon reconstitution and dilution	Final administered dosage form is solution for injection
Active Ingredient	Bortezomib	Bortezomib	Bortezomib	
Bortezomib content	1 mg/mL	2.5 mg/mL	1 mg/mL	Active ingredient
Mannitol	10 mg/mL	25 mg/mL	10 mg/mL	(b) (4)
Water for Injection	(b) (4)		-	
Sodium Acetate (b) (4), USP	*0.82 mg*	*0.82 mg*	-	
Dimethyl Sulfoxide, USP	*20 mg*	*22 mg*	-	
Sodium Hydroxide, NF /Hydrochloric Acid, NF	(b) (4)		-	to adjust the pH
(b) (4)				
pH (reconstitution and dilution of LD)	(b) (4)			Higher than LD
Osmolality (mOsm/kg) after dilution				Higher than LD
Dilution	Not required	Not required	Diluted with sodium hydroxide 0.9%	
Administered Volume	2.34 mL for a 1.8 m^2 BSA human subjects	0.94 mL for a 1.8 m^2 BSA human subjects	2.34 mL for a 1.8 m^2 BSA human subjects	
The recommended starting dose	Will be same using 1 mg/mL solution – Dose is calculated based on the BSA.	Will be same using 2.5 mg/mL solution – Dose is calculated based on the BSA.		Dose is calculated based on the BSA. **1.3 mg/m^2 administered intravenously**

Table 1b: Physicochemical Comparison of Bortezomib (b) (4) Injection, 1 mg/mL and 2.5 mg/mL and the Listed Drug and the *other Approved (Fresenius Kabi NDA 205004)* Product after Reconstitution

Product	Bortezomib Concentration	Administered Volume*	Batch Number (Expiry Date)	pH	Osmolality (mOsmol/kg)
Bortezomib (b) (4) Injection, 1 mg/mL,	1 mg/mL (IV)	2.34 mL (IV)	BORDD1019	5.83	348
			BORDD1029	5.85	346
			BORDD1039	5.80	349
VELCADE (bortezomib) for Injection, 1 mg/mL†	1 mg/mL (IV/SC)	2.34 mL (IV/SC)	225815 (Expiry:9/2020)	5.16	340
			227924 (Expiry: 1/31/2022)	5.59	356
			227926 (Expiry: 3/31/2022)	5.58	351

* Based on a BSA of 1.8 m^2 and a bolus dose of 1.3 mg/m^2
† After reconstitution in 3.5 mL 0.9% sodium chloride
IV = intravenous; SC = subcutaneous

Product	Bortezomib Concentration	Administered Volume*	Batch Number (Expiry Date)	pH	Osmolality (mOsmol/kg)
Bortezomib (b) (4) Injection, 2.5 mg/mL,	2.5 mg/mL (IV)	0.94 mL (IV)	BORCD1019	5.59	472
			BORCD1029	5.56	474
			BORCD1039	5.58	477
VELCADE (bortezomib) for Injection, 1 mg/mL†	1 mg/mL (IV/SC)	2.34 mL (IV/SC)	225815 (Expiry:9/2020)	5.16	340
			227924 (Expiry: 1/31/2022)	5.59	356
			227926 (Expiry: 3/31/2022)	5.58	351
VELCADE (bortezomib) for Injection, 2.5 mg/mL‡	2.5 mg/mL (SC only)	0.94 mL (SC only)	225815 (Expiry:9/2020)	5.43	426
			227924 (Expiry: 1/31/2022)	5.12	444
			227926 (Expiry: 3/31/2022)	5.41	443

Product	Bortezomib Concentration	Administered Volume*	Batch Number (Expiry Date)	pH	Osmolality (mOsmol/kg)
Fresenius Kabi Bortezomib for Injection, 1 mg/mL†	1 mg/mL (IV)	2.34 mL (IV)	6019768 (Expiry:6/30/2021)	5.99	440
			6023056 (Expiry: 11/30/2022)	5.75	433
			C340-013[6]	Not reported	444
					439
					450
			R340-024[6]		435
					439
					430
			R340-025[6]		438
					432
					440

* Based on an average body surface area of 1.8 m^2 and a bolus dose of 1.3 mg/m^2
† After reconstitution in 3.5 mL 0.9% sodium chloride
‡ After reconstitution in 1.4 mL 0.9% sodium chloride
IV = intravenous; SC = subcutaneous

Table 2 provides the unit composition of the proposed product ready to use formulation, Bortezomib Injection 2.5 mg/mL, 1 mg/mL. The drug product is a solution presented at a concentration of 1 mg/mL or 2.5 mg/mL before administration at the recommended dose (No further dilution is required).

Table 2: Unit composition of the proposed product

Listed Drug (VELCADE (bortezomib) for Injection)			MAIA Product (Bortezomib (b) (4) Injection)		
Strength	**1 mg/mL**	**2.5 mg/mL**	**Strength**	**1 mg/mL**	**2.5 mg/mL**
Route	**IV/SC**	**SC**	**Route**	**IV**	**IV**
Ingredient	**Concentration (mg/mL)**		**Ingredient**	**Concentration (mg/mL)**	
Bortezomib	1	2.5	Bortezomib	1	2.5
Mannitol	10	25	Mannitol	10	25
(b) (4)			(b) (4)		
			Sodium acetate (b) (4)	0.82	
			Dimethyl sulfoxide	20	22
(b) (4)			Sodium hydroxide	(b) (4)	
			Hydrochloric acid		
(b) (4)			Water for Injection		

Table 3 provides a side-by-side comparison of the bortezomib concentration in LD and proposed product after reconstitution at Point of Administration.

Table 3: Comparison of bortezomib formulation components in LD and proposed product after reconstitution and dilution prior to administration

Attribute	VELCADE (bortezomib) for Injection (Lyophilized Powder Formulation)	MAIA's Bortezomib (b) (4) Injection (Ready-to-Use Formulation)
Reconstitution Fluid	Only 0.9% Sodium Chloride Injection	Not required
Reconstitution Volume	Intravenous - 3.5 mL† Subcutaneous - 1.4 mL	Not required
Final bortezomib concentration	Intravenous - 1 mg/mL† Subcutaneous - 2.5 mg/mL	1 mg/mL or 2.5 mg/mL for intravenous administration only
Dose administered to patients, based on body surface area (BSA)	1.3 mg/m^2	Same as VELCADE

† Note that the 1 mg/mL concentration may also be used for subcutaneous administration "if local injection site reactions occur following VELCADE administration subcutaneously" at the higher 2.5 mg/mL concentration

BIOWAIVER REQUEST

The Applicant requested a biowaiver of in vivo bioavailability study [21 CFR 320.22] claiming the concentration of proposed drug product after reconstitution and dilution remains same as LD. The Applicant claimed that the active ingredient, route of

administration, dosage form and dosing regimens for the proposed drug product is same as LD.

The proposed drug product is a ready to use solution, intended solely for intravenous administration, therefore its absolute bioavailability is expected to be 100 percent. The LD product is reconstituted and diluted with 0.9% NaCl prior to administration. The Applicant provided comparison of composition and other parameters as discussed below:

1. Formulation composition comparison provided in Table 2 and 3 above

2. Mannitol is present in the formulation [redacted] (b) (4). The difference in mannitol concentration for the proposed 2.5 mg/mL strength is not likely to affect the pharmacokinetics and drug disposition as the product is injected directly by IV administration.

3. Physicochemical comparison of the (concentration 1 mg/mL and 2.5 mg/mL) with the reconstituted and diluted solution of the listed drug

4. In vitro hemolysis study results appear to demonstrate comparable safety and tolerability from the proposed formulation and LD products. The final acceptability of inactive ingredients safety and tolerability will be determined by the non-clinical reviewer. While the Applicant's in vitro study is currently under review by the nonclinical team at the time of this review, the following information is evaluated in support of the bridging between the proposed drug product and the listed drug products from Biopharmaceutics' perspective:

1. Formulation, dosage form
2. Physicochemical data

Reviewer's Assessment: Adequate

The proposed drug product is a parenteral dosage form, ready to use solution for administration as intravenous injection. The proposed drug product has the same active ingredient (bortezomib), has the same dosing regimen, route of administration and indication as the LD. However, due to differences in the inactive ingredients, the application is not eligible for a waiver of in vivo studies MAIA to 21 CFR 320.22(b)(1).

The Applicant submitted data/information to establish a scientific bridge between the proposed drug product, Bortezomib Injection, 2.5 mg/mL for intravenous administration and the listed drug (LD), Velcade® (bortezomib) 3.5 mg/vial in accordance with 21 CFR §320.24(b)(6), based on the following:

- The Applicant provided a comparison of the physicochemical properties of the proposed Bortezomib for Injection and the LD, after reconstitution. The pH and osmolality of the proposed drug product and the LD, after reconstitution (with 0.9 % sodium chloride injection, 1 mg/ml), are similar.
- The proposed product has comparable pH and Osmolality as that of the LD and were not impacted by the difference in inactive ingredients.
- Because the formulations have similar physico-chemical properties [as LD after reconstitution and dilution], the disposition kinetics of bortezomib should be

similar from the proposed [MAIA's Bortezomib Injection, 2.5 mg/mL (3.5 mg in 1.4 mL vial and 2.5 mg in 1 mL vial)] and the LD product, Velcade® (bortezomib) 3.5 mg/vial].

Therefore, based on the totality of the information provided, the proposed drug product is adequately bridged to the listed drug, under 21 CFR 320.24(b)(6), and an in vivo pharmacokinetic study is not needed.

Anitha Palamakula Govada

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	Solution for injection
NDA Number	215331
Assessment Cycle Number	1
Drug Product Name/ Strength	Bortezomib (b) (4) Injection / 1 mg/mL, 2.5 mg/mL
Route of Administration	IV
Applicant Name	Maia Pharmaceuticals
Therapeutic Classification/ OND Division	DHM2
Manufacturing Site	Gland Pharma Limited (b) (4)
Method of Sterilization	

Assessment Recommendation: **Adequate**

Assessment Summary: This review covers sterility assurance for the drug product. No deficiencies have been identified and the submission is adequate for Quality Microbiology.

List Submissions being assessed (table):

Document(s) Assessed	Date Received
eCTD 0001	**9/27/2021**

Highlight Key Issues from Last Cycle and Their Resolution: N/A

Remarks: None

Concise Description of Outstanding Issues: None

Supporting Documents:

- (b) (4).doc, dated 3 February 2017, is referenced (b) (4) (adequate).
- (b) (4).docx, dated 7 April 2020 is referenced (b) (4) (b) (4)

[redacted] (adequate).

- [redacted].docx, dated 24 August 2017, is referenced [redacted] (adequate).
- [redacted].docx, dated 4 August 2020, is referenced [redacted] (adequate).
- [redacted].docx, dated 23 October 2017, is referenced [redacted] (adequate).
- [redacted].docx, dated 6 August 2019, is referenced [redacted] (adequate).

S DRUG SUBSTANCE

N/A. Drug substance is supplied non-sterile.

Assessment: *Adequate*

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

- **Description of drug product –** Sterile, non-pyrogenic solution.

- **Drug product composition –** The composition of the drug product is provided in Table 1, below. For the 2.5 mg/mL formulation, the proposed batch size is [redacted]. For the 1 mg/mL formulation, the proposed batch size is [redacted].

Table 1: Composition of the drug product

Ingredient	Functions	2.5 mg/mL Presentation		1 mg/mL Presentation	
		Quantity/mL (mg)	Quantity/Vial (mg)	Quantity/mL (mg)	Quantity/Vial (mg)
Bortezomib	Active Ingredient	2.5	3.5	1.0	3.5
Mannitol USP	[redacted]	25	35	10	35
Dimethyl Sulfoxide USP		22	30.8	20	70
Sodium Acetate [redacted] USP		0.82	1.15	0.82	2.87
Hydrochloric acid NF		[redacted]			
Sodium Hydroxide NF					
Water for Injection USP					

Table 1 was reproduced from Table 1 in "Description and Composition of the Drug Product," located in Module 3.2.P.1

- **Description of container closure system –**

Table 2: Summary of container-closure system

Component	Description	Manufacturer	DMF No.
Vial	2 mL (b) (4) glass vial, (b) (4) (b) (4) Material Code No. (b) (4)	(b) (4)	(b) (4)
	5 ml (b) (4) glass vial, (b) (4) (b) (4) Material Code No. (b) (4)		
Stopper	13 mm rubber stoppers (b) (4) (b) (4) Material Code No. (b) (4)		
	20 mm rubber stoppers (b) (4) (b) (4) Material Code No. (b) (4)		
Seal	13 mm Aluminum flip off seals with (b) (4) color button Material Code No. (b) (4)		
	20 mm Aluminum flip off seals with (b) (4) color button Material Code No. (b) (4)		

Table 2 was reproduced from Table 3 in "Description and Composition of the Drug Product," located in Module 3.2.P.1

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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R REGIONAL INFORMATION
Executed Batch Records
Executed batch records are provided for 3 lots of each formulation

- 1 mg/mL: BORDD1019, BORDD1029, BORDD1039
- 2.5 mg/mL: BORCD1019, BORCD1029, BORCD1039

Assessment: *Adequate*

2. ASSESSMENT OF COMMON TECHNICAL DOCUMENT – QUALITY (CTD-Q) MODULE 1

2.A. Prescribing Information

Drug product is labeled for single-use with the unused portion to be discarded. Store at 2-8°C or up to (b) (4) at RT once removed from refrigeration.

Assessment: *Adequate*
The applicant has met regulatory expectations with regard to the information related to issues of product quality microbiology that is provided in the product labeling.

MICROBIOLOGY LIST OF DEFICIENCIES
None

Primary Microbiology Assessor Name and Date: Jason M. God, Ph.D., 15 February 2022

Secondary Assessor Name and Date: Julie Nemecek, Ph.D., SPQA, 15 February 2022

Jason God

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