CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218711Orig1s000

PRODUCT QUALITY REVIEW(S)

Title:	NDA IQA Template Title Page- EXEC SUMMARY
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Office of Pharmaceutical Quality

New Drug Application (NDA)
Integrated Quality Assessment Template

NDA Executive Summary

1. Application/Product Information

NDA Number	218711
Applicant Name	ZHUHAI BEIHAI BIOTECH CO LTD
Drug Product Name	BEIZRAY (docetaxel)
Dosage Form	Injection
Proposed Strength(s)	80 mg/4 mL
NDA Classification	Type 5 – New Formulation or New Manufacturer
Route of Administration	Intravenous
Maximum Daily Dose	190 mg (based on 100 mg/m^2, BSA 1.7-1.9 m^2)
Rx/OTC Dispensed	Rx
Proposed Indication	BEIZRAY is a microtubule inhibitor indicated for: • Breast Cancer (BC): single agent for locally advanced or metastatic BC after chemotherapy failure; and with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positive BC (1.1) • Non-small Cell Lung Cancer (NSCLC): single agent for locally advanced or metastatic NSCLC after platinum therapy failure; and with cisplatin for unresectable, locally advanced or metastatic untreated NSCLC (1.2) • Castration-Resistant Prostate Cancer (CRPC): with prednisone in metastatic castration-resistant prostate cancer (1.3) • Gastric Adenocarcinoma (GC): with cisplatin and fluorouracil for untreated, advanced GC, including the gastroesophageal junction (1.4) • Squamous Cell Carcinoma of the Head and Neck (SCCHN): with cisplatin and fluorouracil for induction treatment of locally advanced SCCHN (1.5)
Drug Product Description	BEIZRAY is supplied as a kit consisting of the following: • Two single dose vials of docetaxel injection: 80 mg/4 mL each; a clear, colorless liquid

	• One single dose vial of IV Solution Stabilizer: 50 mL of 25% Human Albumin solution for infusion; a clear and slightly viscous solution		
Co-packaged product information	See above		
Device information	N/A		
Storage Temperature/ Conditions	Store at 20°C to 25°C (68°F to 77°F). Excursions permitted from 15°C to 30°C (59°F to 86°F). [see USP controlled room temperature]. Retain in the original package to protect from light. Protect from freezing.		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Rajan Pragani	Haripada Sarker
	Drug Product/ Labeling	Rajiv Agarwal	Xing Wang/ David Claffey (labeling)
	Manufacturing	Golam Kibria	Kshitij Patkar
	Biopharmaceutics	Hardikkumar Patel	Anitha Govada
	Microbiology	Hemlata Tamta	Denise Miller
	Other (specify)	N/A	
	RBPM	Utkarsh Desai	
	ATL	Xing Wang	
Consults	None		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating:

An expiration dating period of 24 months may be granted when stored at the proposed storage conditions.

b. Additional Comments for Action

None

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

Originally, albumin from (b) (4) was used in the application. Applicant was notified by (b) (4) that they will no longer supply the Albumin for this marketing application; therefore, Applicant provides the LoA from Octapharma. Applicant provides the relevant information using 25% albumin from Octapharma via amendment SDN0019/0020 and updates the relevant sections of the NDA. The data from in vitro studies demonstrated that there is no difference in the overall characteristics between BH009 infusion solution diluting with 25% albumin from Octapharma at 0.14 mg/mL and 0.31 mg/mL of docetaxel concentrations and BH009 infusion solution diluting with (b) (4)% albumin from (b) (4) at (b) (4) mg/mL of docetaxel concentration. It should also be noted that there was no substantial difference between the (b) (4)% and 25% albumin from (b) (4) at (b) (4) mg/mL either. Both Albumins are FDA approved products under BLAs.

The applicant has provided sufficient information to assure the identity, strength, purity, and quality of the proposed drug product. All associated manufacturing, testing, packaging facilities were deemed acceptable based on PAI and previous inspection history. Based on the OPQ review team's evaluation of the information provided in the submission, OPQ recommends APPROVAL of NDA 218711 for BEIZRAY (docetaxel) injection, for intravenous use.

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
Comparability Protocols (PACMP): No
Additional Lifecycle Comments: None

Application Technical Lead Name and Date:
Xing Wang, Ph.D. *10/18/2024*

CHAPTER IV: LABELING (NDA 218711)

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

1.0 PRESCRIBING INFORMATION (ONLY primary secondary labels are needed to complete this review. Cut and paste section 11 and 16 too)

Assessment of Product Quality Related Aspects of the Prescribing Information:

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	Docetaxel
Route(s) of administration	Adequate	For intravenous use
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Adequate	• Two single-dose vials of docetaxel, each contains 80 mg/4 mL docetaxel • One single-dose vial of IV Solution Stabilizer (50 mL, 25% Human Albumin solution)
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored".	N/A	Not applicable
For injectable drug products for parental 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.	N/A	Single-dose
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:	N/A	Not applicable

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

10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).		

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		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the **stability of the reconstituted** or diluted product)	Adequate	Detailed instructions are provided in section 2.10. In-use stability of final infusion solution is provided in 2.11 section.
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food)	N/A	Not Applicable
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	In section 2.10: Prior to administration, visually inspect BEIZRAY final infusion solution for particulate matter or discoloration whenever the solution and container permit. Discard the diluted BEIZRAY infusion solution if the solution is not clear, discolored or appears to have precipitation, it should be discarded. BEIZRAY infusion solution is supersaturated, therefore may crystallize over time. If crystals appear, the solution must be discarded. The BEIZRAY infusion solution should be administered intravenously as a 1-hour infusion under ambient room temperature (below 25℃) and lighting conditions.

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 11).	N/A	Not applicable
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	Not applicable
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	This information is provided in Section 16.3 of the USPI.

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	BEIZRAY is supplied as a kit consisting of the following: • Two single dose vials of docetaxel injection: 80 mg/4 mL each; a clear, colorless liquid • One single dose vial of IV Solution Stabilizer: 50 mL of 25% Human Albumin solution for infusion; a clear and slightly viscous solution
Strength(s) in metric system	Adequate	80 mg/vial
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 (Tablets: 10 mg of drug-x hydrochloride).	N/A	Not applicable
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable	Adequate	Docetaxel: Clear and colorless liquid Albumin: clear and slightly viscous solution
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	Not applicable
For injectable drug products for parental 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.	Adequate	Single-dose

Section 11 (DESCRIPTION)

(b) (4)

[redacted]

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	BEIZRAY, Docetaxel
Dosage form(s) and route(s) of administration	Adequate	BEIZRAY Injection for intravenous use
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)"	N/A	Not applicable
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	Adequate	Yes

<table>
<tr><td>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.</td><td>Adequate</td><td>

BEIZRAY Injection for intravenous use is a sterile, non-pyrogenic, clear colorless liquid, and is available in single-dose vials containing 80 mg (4 mL) docetaxel (anhydrous). Each mL contains 20 mg docetaxel (anhydrous) in 0.770 grams dehydrated alcohol (100% v/v) solution, with citric acid for pH adjustment.
The BEIZRAY kit also contains a single dose vial of IV Solution Stabilizer, 50 mL of 25% Human Albumin solution from Octapharma. 25% Human Albumin solution is a clear, slightly viscous liquid; it is almost colorless or slightly yellow or green. The composition of 25% Human Albumin solution is as follows:

<table>
<tr><th>Component</th><th>Quantity/1000 mL</th></tr>
<tr><td>Protein, of which greater than or equal to 96% is human albumin</td><td>250 g</td></tr>
<tr><td>Sodium</td><td>130 - 160 mmol</td></tr>
<tr><td>Potassium</td><td>less than or equal to 2 mmol</td></tr>
<tr><td>N-acetyl-DL-tryptophan</td><td>0.064 - 0.096 mmol/g protein</td></tr>
<tr><td>Caprylic acid</td><td>0.064 - 0.096 mmol/g protein</td></tr>
<tr><td>Water for Injection</td><td>ad. 1000 mL</td></tr>
</table>
Note: Per 21 CFR 201.100 (b) (5) (iii), labelling includes both qualitative (list of ingredients) and quantitative information (e.g., amounts) about all inactive ingredients except those added to adjust pH or tonicity or water for injection.
</td></tr>
<tr><td>If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol</td><td>N/A</td><td>100% v/v</td></tr>
<tr><td>Sterility statement (if applicable)</td><td>Adequate</td><td>Yes</td></tr>
<tr><td>Pharmacological/Therapeutic class</td><td>Adequate</td><td>Docetaxel is an antineoplastic agent belonging to the taxoid family</td></tr>
<tr><td>Chemical name, structural formula, molecular weight</td><td>Adequate</td><td>Yes</td></tr>
</table>

If radioactive, statement of important nuclear characteristics.	N/A	Not applicable
Other important chemical or physical properties (such as pKa or pH)	Adequate	Yes, it is highly lipophilic and practically insoluble in water

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, include gluten statement (if applicable)	N/A	Not applicable
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity")	N/A	Not applicable
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	Not applicable

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

(b) (4)

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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	Yes
Strength(s) in metric system	Adequate	80 mg/4 mL/vial
Available units (e.g., bottles of 100 tablets)	Adequate	**A kit:** **Docetaxel:** Single-dose vial, individually packaged. **Albumin:** Single-dose vial, individually packaged.
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	Adequate	**Docetaxel:** clear, colorless liquid. **Albumin:** clear and slightly viscous solution
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	Not applicable
For injectable drug products for parental 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.	Adequate	Single-dose

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."	Adequate	Retain in the original package to protect from light. Protect from freezing.

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (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)
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Adequate	Yes
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 natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*	N/A	Not applicable
Include information about child-resistant packaging	N/A	Not applicable

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	**Manufactured by:** Ningbo Shuangcheng Pharmaceutical Co., Ltd. Ningbo, Zhejiang, 315336, China **Distributed by:** Zhuhai Beihai Biotech Co.,Ltd. Zhuhai, Guangdong, 519090, China

2.0 PATIENT LABELING

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

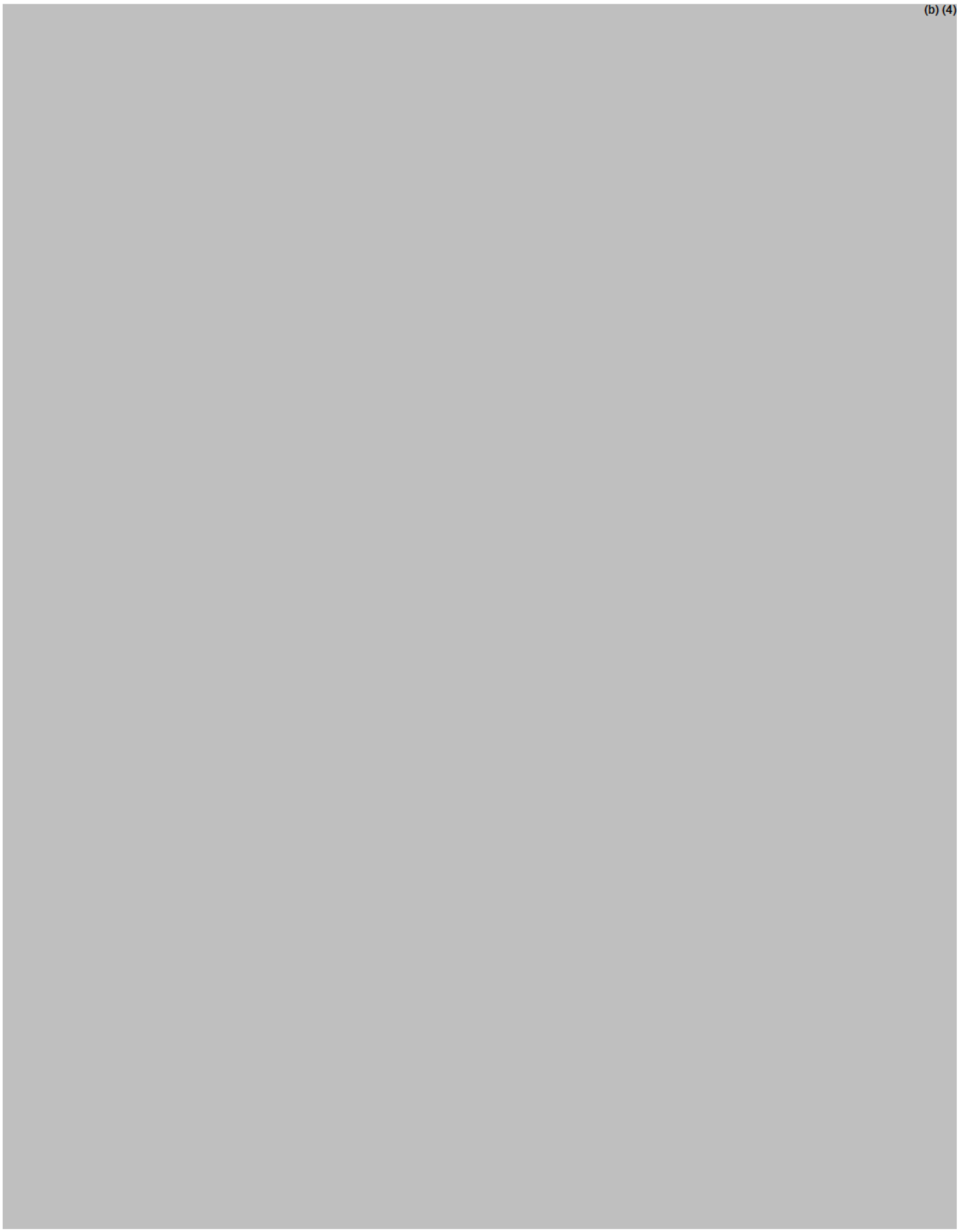
Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[2]	Adequate	BEIZRAY (docetaxel) injection For Intravenous use
Special preparation instructions (if applicable)	N/A	Not applicable (given in hospital setting)
Storage and handling information (if applicable)	N/A	Not applicable (given in hospital setting)
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 differs from the dosage form.	N/A	Not applicable
Active ingredient(s) (if applicable)	Adequate	Yes
Alphabetical listing of inactive ingredients (if applicable)	Adequate	Yes
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer	Adequate	Yes

Any deficiencies should be listed at the end in the "ITEMS FOR ADDITIONAL ASSESSMENT."

[2] Established name = [Docetaxel] [IV] [Injection]

3.0 CONTAINER AND CARTON LABELING

(b) (4)



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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[3], (font size and prominence)	Adequate	Yes
Strength(s) in metric system	Adequate	Yes
Route(s) of administration	Adequate	Yes
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	N/A	N/A
Net contents (e.g., tablet count, volume of liquid)	Adequate	Yes
"Rx only" displayed on the principal display	Adequate	Yes
NDC	Adequate	Yes
Lot number and expiration date	Adequate	Yes
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Adequate	Yes
For injectable drug products for parental 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, and these products require a "Not for direct infusion" statement.	Adequate	Single-dose
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	Provided
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	Adequate	100% v/v
Linear Bar code	Adequate	Yes

3

QUALITY ASSESSMENT

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	Yes
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	Not applicable
No text on Ferrule and Cap overseal, unless a cautionary statement is required.	N/A	Not applicable
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	Not applicable
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	Not applicable
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."***

Proposed edits in the different sections of the PI and the container closure labels were conveyed to the applicant by the OND. Adequate responses to the IRs (dated 9/6/2024) were received on 9/13/2024, 10/2/2024 (Container closure) and 9/20/2024 (PI).

For Information request related to the Container/Closure labels, refer to the APPENDIX

ITEMS FOR ADDITIONAL ASSESSMENT

Assess consistency of product-quality information in prescription drug labeling (PI, c/c labeling, and FDA-approved patient labeling). See Carton/Container Labeling Specific Resources for a presentation about inappropriate inconsistencies of product quality information between labeling.

If there are inappropriate inconsistencies between the labeling (e.g., established name, strength(s), package type term, discard statement, identifying characteristics, storage, reconstitution/dilution instructions), please list these as deficiencies in this section.

Overall Assessment and Recommendation:

- Adequate

Primary Labeling Assessor Name and Date: Rajiv Agarwal 10/3/2024

Secondary Assessor Name and Date: David Claffey, Ph.D

APPENDIX

Information requests: Responses are received on 9/3/2024 and they are adequate.

This is for container label received on 9/13/2024 and their updated carton labeling received on 9/24/24 below.

A. General Comments (Container Label(s) and Carton Labeling)

1. Amend the established name from [redacted] (b) (4) to "(docetaxel) injection" on container and carton labels.

B. Container label

1. Consider un-bold the package type term "4 mL Single-dose Vial Discard Unused Portion" to reduce prominence.

2. On the principal display panel, ensure there is sufficient white space between each statement to improve readability. For example:

3. On the side panel, add "Each mL contains...for pH adjustment" statement.

C. Carton Labeling

1. As currently presented on the principal display panel, the "Discard unused portion" statement is presented in a large and bold font and competes in prominence with other important information (e.g., route of administration). We recommend presenting the "Discard unused portion" statement using the same font type and font size as the "Each Kit Contains:" statement to reduce prominence.

D. We acknowledge your submission dated 9/24/2024 for a mockup of a kit. Provide the amended mockup of kit based on the comments listed above.

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Rajiv Agarwal

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Date: 10/04/2024 08:42:20AM
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David Claffey

Digitally signed by David Claffey
Date: 10/04/2024 02:27:06PM
GUID: 508da71e00029e20b201195abff380c2

CHAPTER VI: BIOPHARMACEUTICS

NDA Number	218711
Assessment Cycle Number	1, ORIG-1 [505(b)(2)]
Drug Product Name/ Strength	Docetaxel Injection, 80 mg/4 mL
Route of Administration	Intravenous (IV)
Applicant Name	Zhuhai Beihai Biotech Co., Ltd.
Therapeutic Classification/ OND Division	Oncology/OND/OOD/Division of Oncology 2
Listed drug	Taxotere® (NDA 020449), Docetaxel Injection, 80 mg/4 mL
Proposed Indication	Breast cancer, Non-small cell lung cancer, Castration-resistant prostate cancer, Gastric adenocarcinoma, and Squamous cell carcinoma of the head and neck

Background: Zhuhai Beihai Biotech Co., Ltd. is seeking approval for Docetaxel Injection, 80 mg/4 mL with the same indications as Taxotere® (docetaxel, DTX, NDA 020449) Injection, the Listed Drug (LD) under the 505(b)(2) regulatory pathway.

Review summary: The proposed drug product (BH009) is a polysorbate 80-free formulation of docetaxel injection. BH009 drug product, 80 mg of Docetaxel in 4 mL is developed as sterile solution for intravenous administration in a single dose vial. The proposed drug product differs from the LD in composition in a vial as follow:

Drug Product Composition of BH009, A Novel Polysorbate 80-Free Formulation of Docetaxel Injection (Comparison Between BH009 and LD)

	BH009 (80 mg/4 mL)	**Taxotere®** (80 mg/4 mL)
Docetaxel	80 mg	80 mg
polysorbate 80	N/A	2160 mg
Ethanol	(b) (4)	1580 mg
Citric acid		N/A

The drug product is supplied with 25% human albumin as a solubilizer. (b) (4) For the preparation of the final infusion solution of BH009, albumin solution is added to 0.9% sodium chloride solution in an infusion bag/bottle, followed by adding BH009 drug product solution with intended clinical dose into the infusion bag/bottle. The docetaxel concentration in the BH009 infusion solution is 0.14 to 0.31 mg/mL. Please refer to drug product label for more information on preparation and administration of the DP.

The LD is provided as single dose vials of Docetaxel 80 mg/4 mL (without human albumin). The required amount of the LD is added into a 250 mL infusion bag or bottle of either 0.9% Sodium Chloride solution or 5% Dextrose solution to produce a final concentration of 0.3 mg/mL to 0.74 mg/mL using syringe.

The Applicant has provided bioequivalence study data between the proposed drug product and the LD (to be assessed by the Office of Clinical Pharmacology) and Ethanol safety assessment (to be assessed by the OND's nonclinical review team). Because the drug product is a solution for injection, in vitro drug release testing is not required for batch release or stability testing of the proposed drug product. In addition, adequate controls for the drug product quality assurance (pH, osmolarity, assay etc.) are included in the drug product batch release specifications (to be assessed by the OPQ's drug product and manufacturing process review teams).Therefore, Biopharmaceutics review is not necessary for this NDA.

Note: The Applicant has proposed a change in excipient manufacturing source i.e. a new supplier for solubilizer (human albumin). It should be noted that Human Albumin has an approved Biologics License Application (BLA) and specifications for batch release. Therefore, a change in albumin source (excipient manufacturer) is not expected to impact the drug product quality and drug substance (b) (4)

OVERALL REVIEW RECOMMENDATION: The drug product is a solution for injection, from a Biopharmaceutics perspective, there are no approvability issues. Final determination of bioequivalence between the proposed and LD product is deferred to Clinical, Clinical Pharmacology, Non-Clinical and other CMC disciplines.

Primary Biopharmaceutics Assessor's Name and Date: Hardikkumar H Patel, Ph.D., 6/18/2024

Secondary Assessor Name and Date (and Secondary Summary, as needed): Anitha Govada, Ph.D.,6/18/2024

Hardikkumar Patel

Digitally signed by Hardikkumar Patel
Date: 8/14/2024 01:17:34PM
GUID: 5435662600016f7b78898063ba9a457e2

Anitha Palamakula Govada

Digitally signed by Anitha Palamakula Govada
Date: 8/14/2024 01:18:53PM
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U.S. FOOD & DRUG ADMINISTRATION

CHAPTER VII: MICROBIOLOGY

Product Information	Indicated for treatment of breast cancer. RLD is TAXOTERE (Docetaxel injection) NDA 020449
NDA Number	218711
Assessment Cycle Number	1
Drug Product Name/ Strength	Docetaxel Injection (Albumin solubilized), 80mg/4mL
Route of Administration	Intravenous infusion
Applicant Name	Zhuhai Beihai Biotech Co. Ltd.
Manufacturing Site	Ningbo Shuangcheng Pharmaceutical Co. Ltd. No. 866 BinHai Fourth Road, Hangzhou Bay New Zone, Ningbo Zhejiang, China
Method of Sterilization	(b) (4)

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: N/A

Assessment Summary: *Docetaxel Injection, 80 mg/ 4 mL is* (b) (4)

(b) (4)

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
001	10/06/2023
0013	03/12/2024
0019	05/17/2024
0022	05/29/2024

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

Remarks: This is an eCTD submission. Information request was conveyed to the applicant on 08/18/2024 and the response was received on 03/12/2024.

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

Supporting Documents:

- Microbiology review [redacted].doc dated 02/03/2023 (adequate) for [redacted]
- Microbiology review [redacted]docx dated 08/21/2023. (adequate) for [redacted]
- Biologic License Application (BLA) STN 125154 for 25% Human Albumin.

Select Number of Approved Comparability Protocols: 0

S DRUG SUBSTANCE

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

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

(3.2.P.1 Description and Composition of the Drug Product.pdf)

- **Description of drug product –** Docetaxel injection, 80mg/4mL is a sterile, non-pyrogenic solution for intravenous administration.
- **Drug product composition –**

Components	Unit formula		Quality Reference	Function
	mg/unit	%, w/w		
Docetaxel	80 mg	[redacted]	USP	Active ingredient
Citric acid anhydrous	[redacted]	[redacted]	USP	pH adjustment
Dehydrated Alcohol	[redacted]	[redacted]	USP	[redacted]
Total weight (mg)	[redacted]	100%	-	-

Drug product is co-packaged with a diluent in a kit for proposed clinical use. The diluent is 25% Human Albumin solution for infusion. Albumin (Human) 25% supplied and marketed in the US by Octapharma Pharmazeutika Produktionsges.m.b.h. is an approved product under US Biologic License Application BLA STN 125154. Letter of Authorization dated 04/12/2024 from Octapharma Pharmazeutika Produktionsges.m.b.h. was provided. Biological drug products such as Albumin (Human) 25% are regulated by Center for Biologics Evaluation and Research (CBER). There are no product quality microbiology concerns at this time.

Note to reviewer: In the original submission the drug product was co-packaged with a diluent in a kit for proposed clinical use. The diluent was (b) (4)% or 25% Human Albumin solution for infusion (b) (4) marketed in US under (b) (4) In submission dated 05/17/2024, the applicant stated that they will not use albumin from (b) (4) for future commercial manufacturing.

- **Description of container closure system –**

Component	Description	Manufacturer
Glass vial	10 mL/20 mm colorless (b) (4) glass vial	(b) (4)
Stopper	20 mm (b) (4) rubber stopper	
Stopper	20 mm (b) (4) rubber stopper	

Exhibit Batches: (b) (4)
Proposed Commercial Batch Size: (b) (4)

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

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

23 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

Hemlata Tamta

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Date: 6/24/2024 11:12:14AM
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Denise Miller

Digitally signed by Denise Miller
Date: 6/25/2024 08:17:13AM
GUID: 508da7280002a5d546459b998253d1aa

Xing Wang

Digitally signed by Xing Wang
Date: 10/18/2024 09:26:16AM
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/s/

XING WANG
10/18/2024 09:37:04 AM