CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

220787Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary
Review cycle 01

1. Application/Product Information

NDA Number	220787		
Applicant Name	Wockhardt BIO AG		
Drug Product Name	ZAYNICH* (cefepime and zidebactam) for injection		
Dosage Form	Powder for solution (for injection)		
Proposed Strength(s)	3 grams/vial (2 grams of cefepime and 1 gram of zidebactam)		
Route of Administration	Intravenous		
Maximum Daily Dose	6 grams of cefepime and 3 grams of zidebactam		
Rx/OTC Dispensed	Rx		
Proposed Indication	Treatment of patients 18 years of age and older with complicated urinary tract infections (cUTI) including pyelonephritis, with and without concurrent bacteremia.		
Drug Product Description	White to pale yellow sterile powder		
Co-packaged product information	N/A		
Device information	N/A		
Storage Temperature/ Conditions	Refrigerated at 2°C to 8°C (36°F to 46°F); excursions are permitted to 25°C (77°F). Retain the vial in the outer carton prior to and after reconstitution to protect it from light.		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Karina Zuck	Katherine Windsor
	Drug Product	*Jessica Zarenkiewicz*	Akshata Nevrekar
	Drug Product Labeling	*Jessica Zarenkiewicz*	David Claffey

	Manufacturing	Mirtha Millones	Bo Jiang
	Biopharmaceutics	*N/A*	*N/A*
	Microbiology	Shannon Heine	Neal Sweeney
	Other (specify)	N/A	N/A
	RBPM	Janell Artis	
	ATL	Akshata Nevrekar	
Consults	N/A		

* The drug product name is pending DMEPA review

2. Final Overall Recommendation - <u>Approval with PMCs</u>

3. Action Letter Information

a. Expiration Dating: Based on the stability data submitted to date, the expiry dating period for ZAYNICH (cefepime and zidebactam) for injection shall be 24 months from the date of manufacture when stored refrigerated at 2°C to 8°C (36°F to 46°F) with brief excursions permitted up to 25°C (77°F). The vial should be retained in the outer carton prior to and after reconstitution to protect it from light.

b. Additional Comments for Action:
<u>The following Post-Marketing Commitments (PMC) should be included in the action letter:</u>

<u>PMC #4999-4: Drug product review team</u>

Method revalidation studies for the analytical procedure used for the determination of (b) (4) (b) (4), and submission of results of the revalidation of the analytical method after incorporation of internal reference standard. Report on method equivalency comparing the results of the existing method and the revalidated method for the determination of (b) (4).

Final Report: September 2026

The final report should be submitted as a prior approval supplement.
The final report submission should be identified as “Final Report Submission for PMC 4999-4” in addition to being identified as a “Prior Approval Supplement”.

<u>PMC #4999-5: Joint PMC between Drug Product and Non-clinical review team</u>

Submission of results of the leachable impurity assessment on the 21-month long-term stability samples from three registration drug product batches. Any leachables present

above the Safety Concern Threshold (SCT) of 5 mcg/day will be identified. Toxicological risk assessments and permitted daily exposure (PDE) values for all identified leachables occurring at levels that exceed (b) (4) mcg/mL corresponding to a daily exposure of 5 mcg/day will be provided. PDE determinations will follow the recommended methods described in the ICH Q3C(R9) and ICH Q3D(R2) guidances and full method details for each PDE determination will be submitted to the FDA, including all PDE calculations, determinations of LOELs, NOELs, and uncertainty factors, and the sources of all supporting literature and/or study findings.

Final Report: July 2026

The final report should be submitted as a prior approval supplement.
The final report submission should be identified as “Final Report Submission for PMC 4999-5” in addition to being identified as a “Prior Approval Supplement”.

PMC #4999-6: Joint PMC between Drug Product and Process review team

Three batches of the drug product will be manufactured at the target fill weight of (b) (4) of the labeled claim and with (b) (4) individual fill weight specification limits, including evaluation of low filling speed of (b) (4) VPM in one batch and high filling speed of (b) (4) VPM in a separate batch.

Final Report: January 2027

The following information will be submitted to the Agency for three batches:

- Drug product release testing data for all three batches
- An Excel spreadsheet with individual fill weight results, mean, and standard deviation for each IPC check, and statistics summary for the fill weight data including all the rejected units for each batch
- Chronological and distribution plots of the individual fill weight results
- Process capability analysis with respect to the proposed LSL/USL of (b) (4), including both Cpk and Ppk calculation using “Sigma within” and “Sigma total”, respectively.
- Tentative filled vial rejection limit based on available batch data will be included in the intended MBR. Excursions beyond the proposed limit will be investigated to identify the root cause. The tentative rejection limit will be finalized based on manufacturing batch data from a statistically significant number of commercial batches.

The final report should be submitted as a prior approval supplement.
The final report submission should be identified as “Final Report Submission for PMC 4999-6” in addition to being identified as a “Prior Approval Supplement”.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

This NDA provides for a 505(b)(2) application of cefepime and zidebactam, to be indicated for patients 18 years of age and older with complicated urinary tract infections (cUTI) including pyelonephritis, with and without concurrent bacteremia.
The Applicant has developed an injectable dosage form for intravenous administration referring to Maxipime (cefepime for injection (NDA 050679) as the Listed Drug (LD) for this application. The LD is discontinued (not discontinued or withdrawn for safety or effectiveness reasons) in US, manufactured by Hospira Inc.

OPQ recommends ***an approval of NDA 220787*** ZAYNICH* (cefepime and zidebactam), for injection 3 grams/vial (2 grams of cefepime and 1 gram of zidebactam) *packaged in a single dose glass vial. The overall manufacturing inspection recommendation for this NDA is* ***Approve,*** *as entered in Panorama by the Office of Pharmaceutical Manufacturing Assessment (OPMA) on May 14, 2026.*

Drug Substance: Adequate
Cefepime for injection, USP, is a sterile dry mixture of cefepime hydrochloride, USP (sterile bulk) and L-arginine. The applicant cross references the CMC information for cefepime for injection (sterile bulk) drug substance to DMF (b) (4) which was last reviewed (b) (4) and found adequate by Dr. J. Nogueira from the CMC perspective and (b) (4) by Dr. D. Bridge from the microbiology perspective.
Zidebactam is a white to pale yellow powder. The quality information for zidebactam is submitted in the NDA and found Adequate.
The NDA includes supportive information for the drug substance batches used in the manufacture of the proposed drug product, including a nitrosamine risk assessment. The (b) (4) of the zidebactam is controlled in the drug substance specification.
The information submitted for the drug substance is found to be adequate on May 5, 2026 (Refer to the Drug Substance review).

Drug Product: Adequate with PMCs
The drug product is a sterile, single-dose powder for injection for intravenous use. Each vial contains two grams of cefepime (present as cefepime hydrochloride monohydrate) and one gram of zidebactam (present as zidebactam dihydrate). L-arginine is added to the formulation (b) (4). The cefepime hydrochloride is provided to the drug product manufacturer (b) (4) (b) (4).

The drug product is a white to pale yellow powder packaged in a 50 mL USP Type I clear glass vial with a 20 mm (b) (4) rubber stopper and 20 mm flip-off seal. The maximum daily dose is three vials of drug product (one vial every eight hours) corresponding to a total dose of six grams of cefepime and three grams of zidebactam.

The drug product manufacturing consists of (b) (4). An overfill (b) (4) has been included in the vial to allow

withdrawal of complete labelled dose and to align with the manufacturing capability of the filling process and assay of the drug substance on as is basis.

The proposed drug product is to be reconstituted with Sterile Water for Injection, 0.9% Sodium Chloride, 5% Dextrose, and Lactated Ringer's solution. The reconstituted product is further diluted with 0.9% Sodium Chloride, 5% Dextrose, and Lactated Ringer's solution. The compatibility and stability information for the drug product with the proposed reconstitution agents and diluents was found adequate to support the administration and in-use storage instructions in the prescribing information (PI).

From a drug product quality perspective, the submitted information on the drug product composition, physical stability, compatibility with proposed diluents, specifications, analytical methods, nitrosamine risk assessment, (b) (4) elemental impurities, container closure system, and stability data were reviewed and found acceptable.
The information submitted for the drug product is found to be adequate on May 20, 2026 (Refer to the Drug Product review).

However, there are several issues that will be addressed through additional PMCs. During the review cycle, nitrosamine testing was added to the drug product specification, and the testing is proposed to be conducted at a facility different from the facility used for method development. Due to the proposed method transfer and based on advice from the Agency for optimization of the analytical method, method revalidation utilizing an internal reference standard will be conducted at the new testing site. Method equivalency report comparing the results of the existing method and the revalidated method for determination of (b) (4) will confirm that the results submitted remain reliable (PMC 1).
An interim report was provided during the review cycle with leachable impurity testing data using samples from the 21-month stability time point to support the proposed shelf-life. The interim report had incomplete assessment for all potential leachable impurities in the drug product. This PMC # 2 requests a final study report with comprehensive leachable impurity testing data and supportive non-clinical data for any identified leachable impurity above the Safety Concern Threshold (SCT).

As a part of PMC #3 from OPMA review team, release data from three new batches of the drug product manufactured to support the proposed overfill (b) (4) is required from a drug product perspective.
(Refer PMCs above with final report submission timelines)

Labeling: <u>Adequate</u>
The proposed quality related labeling information, which includes detailed drug product preparation and administration instructions, container labels, and carton labeling have been found adequate and meet the regulatory requirements.
(Refer to the Quality Labeling review)

Biopharmaceutics: N/A

Microbiology: <u>Adequate</u>

The information submitted for microbiology is found adequate on March 4, 2026 (Refer to the Microbiology review).

Process: Adequate with PMCs

The manufacturing process consists of (b) (4) (b) (4)

The overall information submitted for the drug product manufacturing was found adequate on 5/18/2026 (Refer to process and facility review in Panorama)

The original registration batches were manufactured at target fill weight (TFW) of (b) (4) of the labeled claim, with individual fill weight limits to (b) (4) of the TFW In response to FDA quality deficiencies the firm revised the TFW to (b) (4) of the labeled claim and individual fill weight limits to (b) (4) of the TFW with no supporting batch data provided. Therefore, a PMC is issued to request additional batch manufacturing data to demonstrate that the (b) (4) process is adequately controlled with the revised target fill weight and (b) (4) fill weight limits. (Refer PMC #3)

Facilities: Adequate

The overall manufacturing inspection recommendation for this NDA is **Approve,** as entered in Panorama by the Office of Pharmaceutical Manufacturing Assessment (OPMA) on May 14, 2026.

Summary:

The information submitted for the drug substance, drug product, manufacturing process, microbiology and facilities is adequate for this review cycle. However, there are several issues that will be addressed through additional PMCs. These issues include revalidation of the analytical method transferred to a new site for testing along with submission of method equivalency data between the existing method and the new method (PMC# 4999-4). Submission of a final report for leachable impurity assessment in the drug product batches nearing expiry (PMC# 4999-5) and manufacturing new drug product batches at the proposed overfill (b) (4)) and revised (b) (4) limits and submission of all process and drug product release data for the same (PMC# 4999-6). (Please refer to PMCs above)

Therefore, OPQ recommends an Approval (with PMCs) of NDA 220787 for ZAYNICH* (cefepime and zidebactam) for injection packaged in a single dose glass vial.

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

Recommendation by Subdiscipline:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate with QPAs**
Quality Labeling	**-**	**Adequate**

Manufacturing	**-**	**Adequate with QPAs**
Biopharmaceutics	**-**	**N/A**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): No

5. **Life-Cycle Considerations**
   Established Conditions per ICH Q12: No
   Comments:

   Comparability Protocols (PACMP): No
   Comments:

   Additional Lifecycle Comments: N/A

Application Technical Lead Name and Date: Akshata Nevrekar; 5/20/2026

Akshata Nevrekar

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CHAPTER IV: LABELING

For more details about the items in this template, please see Chapter IV (Labeling) of the NDA IQA Guide (OPQ-ALL-WI-0006)

NDA Number	220787
Assessment Cycle Number	1
Drug Product Name	ZAYNICH (cefepime and zidebactam) for injection, for intravenous use 3 g/vial

Assessment Recommendation: Adequate pending labeling negotiations

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Adequate	Adequate pending revisions to be communicated
Patient Information	N/A	
Instruction for Use (IFU)	N/A	
Container Labels	Adequate	Adequate pending revisions to be communicated
Carton Labeling	Adequate	Adequate pending revisions to be communicated

Brief Description of Outstanding Issues: see comments communicated via the Prescribing Information.

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
0001, 1	9/30/2025	PI and Carton/Container Label
0011, 11	12/19/2025	Revised PI

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

[redacted]

[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)

Reference ID: 5801666

(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]	Inadequate	Order needs to be "cefepime and zidebactam" throughout. Comment sent for applicant to make this change
Route(s) of administration	Adequate	
Controlled drug substance symbol (if applicable)	N/A	
Initial U.S. Approval [§201.57(a)(3)]	Adequate	
Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		
Dosage form(s)[4] and strength(s) in metric system[5]	Adequate	
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	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	N/A	

[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
[7] Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (March 2013)

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)
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]	Adequate	

Assessment: *Inadequate*

See comment regarding order of drug substances.

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(b) (4)

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

[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)
DOSAGE AND ADMINISTRATION section		
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	
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	
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]	Adequate	
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*	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)
applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs."		

Assessment: *Inadequate*

See revisions in red and via the sharepoint document

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	
Strength(s) in metric system	Adequate	
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	
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	
Assess if the tablet is scored. If product meets guidelines and	N/A	

[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)
criteria for a scored tablet, state "functionally scored."		
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>).	Adequate	

Assessment: *Inadequate*

See revisions in red and via the sharepoint document.

1.2.3 Section 11 (DESCRIPTION)[14]

Shown below as originally proposed. See sharepoint document for recommended edits:

(b) (4)

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

[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	
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	
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)].	Adequate	
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	
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)].	Adequate	
If alcohol is present, must provide the amount of alcohol in	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)
terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].		
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	Adequate	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Inadequate	Pharmacological class of zidebactam revised following internal discussion. See sharepoint document.
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	
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	
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	

[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)

Assessment: *Inadequate*

See revisions in red and via the sharepoint document.

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

(b) (4)

[redacted]

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

Reference ID: 5801666

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	
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	
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	
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	
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>).	Inadequate	See edit in red

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 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)]	Adequate	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	
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."*[21]	N/A	
Include information about child-resistant packaging[22] (if chosen by manufacturer).	N/A	

[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)

Assessment: *Inadequate*

See revisions in red and via the sharepoint document.

1.2.5 Other Sections of Labeling

Not applicable

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

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	

Assessment: *Adequate*

2.0 PATIENT LABELING

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

No additional labeling proposed

3.0 CONTAINER AND CARTON LABELING[24]

[23] § 201.1(h)(5) and 201.1(i); Labeling Review Tool (March 2022, page 74)
[24] Carton and Container Labeling Resources

3.1 Container Labels[25]

(b) (4)

3.2 Carton Labeling

(b) (4)

[25] 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.

Reference ID: 5801666

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[26], (font size and prominence) [§ 201.10(g)(2)].	Inadequate	Yes	Order should be "cefepime and zidebactam". Comment sent to applicant for order switching
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[27]	Adequate	Yes	
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	Adequate	Yes	
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	
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[28]	Adequate	Yes	
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Adequate	Yes	
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	Yes	
Lot number and expiration date [§ 201.18 & 201.17].	Adequate	Yes	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	Yes	

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

[27] 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)

[28] § 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)
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, and these products require a "Not for direct infusion" statement. (See USP <659>).	Adequate	Yes	
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)].	Adequate	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)].	Adequate	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	Choose an item.	
Linear Bar code [§ 201.25(c)(2)].[29]	Adequate	Yes	
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	Yes	

[29] 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)
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	Yes	
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	N/A	Choose an item.	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	Choose an item.	
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	Adequate	Choose an item.	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	Choose an item.	
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.[30]	N/A	Choose an item.	
And others if space is available.	N/A	Choose an item.	

[30] USP General Notices 3.20 Indicating Conformance

Assessment of Carton Labels and Container Labeling: *Inadequate*

Order of active ingredients in the name should be reversed. This comment is to be communicated with other PI revisions.

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

Labeling comments to be communicated to the Applicant by 4/29. The labeling is expected to be adequate at the conclusion of labeling negotiations.

Primary Labeling Assessor Name and Date: Jessica Zarenkiewicz

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

Reference ID: 5801666

Jessica Zarenkiewicz

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Date: 4/28/2026 01:51:18PM
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David Claffey

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U.S. FOOD & DRUG ADMINISTRATION

CHAPTER VII: MICROBIOLOGY

IQA ANDA Assessment Guide Reference

Product Information	
NDA Number	220787
Assessment Cycle Number	1
Drug Product Name / Strength	WCK 5222 [Zidebactam (WCK 5107) and Cefepime] for Injection / 3 g/vial contains 1 gram of Zidebactam and 2 grams of Cefepime
Route of Administration	Intravenous injection
Applicant Name	Wockhardt BIO AG
Therapeutic Classification/ OND Division	Classification Unknown / CDER/OND/OID/DAI
Manufacturing Site	ACS Dobfar S.p.A. Via Alessandro Fleming 2, Verona 37135, Italy (ITA)
Method of Sterilization	Aseptic fill of sterile bulk API

Assessment Recommendation: **Adequate**

Assessment Summary:

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
Seq 0001 (1)	30 September 2025
Seq 0018 (18)	23 January 2026
Seq 0025 (25)	17 February 2026
Seq 0029 (29)	27 February 2026
Seq 0031 (31)	13 March 2026
Seq 0038 (38)	20 March 2026
Seq 0046 (46)	13 April 2026

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

Remarks: The subject drug is a sterile single-dose vial white to pale yellow

powder combination of zidebactam and cefepime for Injection, for intravenous administration indicated for the or the treatment of patients 18 years of age and older with complicated urinary tract infections. Cefepime for Injection and Zidebactam Sterile are filled aseptically into 50 mL USP clear type I (b) (4) glass vial with 20 mm neck, stoppered with 20 mm (b) (4) rubber stopper and sealed with 20 mm flip-off seal (b) (4). The applicant provided an LoA from (b) (4) for DMF (b) (4) for Cefepime for Injection (Sterile Bulk), dated 25 September 2025. The application was granted priority review status. Product Quality deficiencies were conveyed to the applicant in multiple Information Requests.

The submission is recommended for approval from the standpoint of product quality microbiology.

Concise Description of Outstanding Issues: N/A

Supporting Documents:

- Type II DMF (b) (4) in regard to the Cefepime for Injection (Sterile Bulk) manufacture.
- Microbiology Review of DMF (b) (4) (b) (4) (b) (4).
- Type III DMF (b) (4) (b) (4)
- Microbiology Review of DMF (b) (4) (b) (4)

Select Number of Approved Comparability Protocols: 0

S DRUG SUBSTANCE

The subject drug product consists of two sterile drug substances filled aseptically (b) (4) (b) (4) into a single vial.

Cefepime for Injection:

Letter of Authorization (LoA) for DMF # (b) (4)

The applicant provided an LoA from (b) (4) dated 25 September 2025, for DMF# (b) (4) in regard to the Cefepime for Injection (Sterile Bulk) manufacture.

The manufacturing process for the sterile drug product was reviewed for sterility assurance and found inadequate. Therefore, the following deficiency was sent to the applicant on 6 January 2026.

Type II DMF (b) (4) has been reviewed in support of manufacturing Cefepime for Injection (Sterile bulk) and found inadequate. The DMF holder has been notified.

Summary of the applicant's response dated 23 January 2026:

(See *Cover Letter-0018-01232026*)

The applicant states that the DMF holder informed them that the information request received on DMF (b) (4) was responded to on 20 January 2026. This information was assessed.

Assessment: *Adequate*
The manufacturing process for the sterile Cefepime for Injection drug substance was reviewed for sterility assurance and found adequate in Microbiology Review of DMF (b) (4) (b) (4).

(b) (4)

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(b) (4)

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

- **Description of drug product**
  (See *Description and Composition of the Drug Product*)
  The finished drug product, WCK 5222 (zidebactam and cefepime) for Injection, is a sterile single-dose vial combination containing 1 gram of Zidebactam and 2 grams of Cefepime for intravenous administration. The product is a white to pale yellow powder for reconstitution with 0.9% Sodium Chloride Injection, 5% Dextrose Injection, Lactated Ringer's solution, or sterile Water for Injection. It is packed in a 50 mL USP clear type I (b) (4) glass vial, stoppered with a 20 mm (b) (4) rubber stopper, and sealed with a 20 mm flip-off seal.
- **Drug product composition**

Component	Quantity/unit dose	Function

Cefepime Hydrochloride (b) (4)	(b) (4) g* (equivalent to 2 g Cefepime)	Active Ingredient
L-arginine	1.4 g	pH adjuster
Zidebactam (b) (4)	(b) (4) 1 g zidebactam)	Active Pharmaceutical Ingredient (Beta-Lactamase Inhibitor)
(b) (4)		

- **Description of container closure system**

(See *Container Closure System*)

Component	Description	Supplier
Container	50 mL (b) (4) mL overfill capacity) clear (b) (4) glass vial with 20 mm neck (USP Type I)	(b) (4)
Closure	20 mm (b) (4) rubber stoppers (b) (4) (b) (4)	
Seal	20 mm (b) (4) aluminum over-seal with (b) (4) plastic flip-off cap. Batch number is printed on the skirt surface of each ferrule/aluminum over-seal	

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

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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MICROBIOLOGY LIST OF DEFICIENCIES

None.

Primary Microbiology Assessor Name and Date: Shannon Heine, PhD, 14 April 2026
Secondary Assessor Name and Date: Neal Sweeney, PhD, 14 April 2026
"I concur."

Reference ID: 5801666

Shannon Heine

Digitally signed by Shannon Heine
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Neal Sweeney

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Date: 4/14/2026 02:53:46PM
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/s/

AKSHATA A NEVREKAR
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