CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

220305Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number.	220305
Applicant Name	Kura Oncology, Inc.
Drug Product Name	KOMZIFTITM (ziftomenib) capsules
Dosage Form.	Capsules
Proposed Strength(s)	200 mg
Route of Administration	Oral
Maximum Daily Dose	600 mg
Rx/OTC Dispensed	Rx
Proposed Indication	KOMZIFTI is a menin inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a nucleophosmin 1 (NPM1) mutation.
Drug Product Description	The ziftomenib drug product is supplied as immediate release, size 00 capsules for oral administration. The capsules are packaged in sealed high density polyethylelene (HDPE) bottles with a child resistant cap. The Applicant is planning to market only 90's count configuration (submission dated 08/21/2025)
Co-packaged product information	N/A
Device information:	N/A

Storage Temperature/ Conditions	Store at USP controlled room temperature 20°C to 25°C (68°F to 77°F). Excursions permitted between 15°C and 30°C (59°F to 86°F).		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Kabir Shahjahan	Haripada Sarker
	Drug Product/ Labeling	Damien Duveau	Shalini Anand/David Claffey
	Manufacturing	Quamrul Majumder	Christine Falabella
	Biopharmaceutics	Alaadin Alayoubi	Anitha Govada
	Microbiology	N/A	N/A
	Other (specify):	N/A	N/A
	RBPM	Janell Artis	
	ATL	Shalini Anand	
Consults	N/A		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: An expiration dating period of **30 months** is granted for the drug product when stored and transported at 2°C to 8°C (36°F to 46°F). After receipt, patient may store at room temperature 20°C to 25°C (68°F to 77°F). Do NOT exceed 30°C (86°F).

b. Additional Comments for Action: n/a

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

OPQ recommends ***APPROVAL*** of NDA 220305 for the commercialization of KOMZIFTITM (ziftomenib) capsules. Based on our evaluation of the available information, the Applicant

provided sufficient information to support an approval recommendation from the drug product quality perspective. The Applicant provided adequate information on the proposed drug product to ensure the identity, strength, purity, and quality of the proposed drug product. The overall manufacturing inspection recommendation is approval for all the facilities associated with this application. The proposed labeling and labels include adequate information to meet the regulatory requirements.

a. 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	**-**	**N/A**

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

2. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments:

Comparability Protocols (PACMP): No

Comments: N/A

Additional Lifecycle Comments: N/A

Shalini Anand

Digitally signed by Shalini Anand
Date: 9/30/2025 09:52:56AM
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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	220305
Assessment Cycle Number	01
Drug Product Name	KOMZIFTI (Ziftomenib capsule, 200 mg)

Assessment Recommendation: Choose an item.

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Adequate	SDN 31
Patient Information	Adequate	N/A
Instruction for Use (IFU)	N/A	N/A
Container Labels	Adequate	SDN 23
Carton Labeling	N/A	No carton labeling submitted.

Brief Description of Outstanding Issues: None

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
eCTD # 0001, SDN # 01	03/31/2025	USPI, bottle label
eCTD # 0023, SDN # 23	08/01/2025	Revised text on the bottle label. Clarification on the count packaging configuration.
eCTD # 0031, SDN # 31	08/21/2025	Revised bottle label

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

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

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

[redacted]

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights[2] [21 CFR 201.57(a)(2)]		
Established name(s)[3]	Adequate	KOMZIFTI™ (ziftomenib) capsules, for oral use
Route(s) of administration	Adequate	Oral use
Controlled drug substance symbol (if applicable)	N/A	
Initial U.S. Approval [§201.57(a)(3)]	Adequate	Initial U.S. approval:
Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		

[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).

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 form(s)[4] and strength(s) in metric system[5]	Adequate	Capsules, 200 mg.
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).[6]	N/A	The API is the free base
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	N/A	N/A
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.[8]	N/A	N/A

Assessment: *Adequate*

[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)
[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>

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(b) (4)

[redacted]

[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)

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		
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	Administer KOMZIFTI once daily fasted with water at least 1 hour before or 2 hours after a meal.
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	Swallow capsules whole. Do not open, break, or chew the capsules.
For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11]	N/A	N/A
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable	N/A	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)
to another section of the PI (e.g., Section 11).		
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	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."	N/A	N/A

Assessment: *Adequate*

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

Capsules of ziftomenib are available in 200 mg strength. The capsules are white, and are imprinted with "ZIF 200" in black ink.

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	Capsule, 200 mg
Strength(s) in metric system	Adequate	N/A
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	N/A	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)
of drug-x hydrochloride). No equivalency statement.		
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	The mention of (b) (4) (b) (4) should be removed as it is unnecessary.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	N/A
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	N/A

Assessment: *Adequate*

1.2.3 Section 11 (DESCRIPTION)[14]

(b) (4)

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

(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)
DESCRIPTION section		
Proprietary and established name(s)[15] [§ 201.57(c)(12)(i)(A)].	Adequate	KOMZIFTI (ziftomenib)
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	The drug product is presented as a 200 mg capsule for oral administration.
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	N/A	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).

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)
of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].		
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	Excipients should be listed in alphabetical order.
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	N/A
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	N/A
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	N/A
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	Menin inhibitor
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	The chemical name is (S)-4-methyl-5-((4-((2-(methylamino)-6-(2,2,2-trifluoroethyl)thieno[2,3-d]pyrimidin-4-yl)amino)piperidin-1-yl)methyl)-1-(2-(4-

[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.

[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).

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)
		(methylsulfonyl)piperazin-1-yl)propyl)-1H-indole-2-carbonitrile.
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	N/A
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	Adequate	Ziftomenib is a white to off-white powder and is highly soluble in aqueous solution at pH 1.2 and practically insoluble at pH ≥ 4.
For oral prescription drug products, include gluten statement[19] (if applicable).	N/A	No gluten in the formulation.
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity").	N/A	N/A
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	N/A

Assessment: *Adequate*

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

(b) (4)

[redacted]

[19] Draft guidance: *Gluten in Drug Products and Associated Labeling Recommendations* (December 2017)
[20] See § 201.57(c)(17); Labeling Review Tool (March 2022, page 70). Consider including proprietary name and established name.

(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)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s) [§ 201.57(c)(17)].	Adequate	200 mg is the only dosage form.
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	N/A
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Inadequate	(b) (4) (b) (4) Provide the NDC code for each packaging configuration.
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	The mention (b) (4) should be removed as it is not necessary.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	N/A
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	N/A

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs." [§ 201.57(c)(17)(iv)]	N/A	No special handling instruction. The drug product is not light or moisture sensitive.
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	List storage temperature in Celsius first, then in Fahrenheit between parentheses.
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	N/A
Include information about child-resistant packaging[22] (if chosen by manufacturer).	Adequate	KOMZIFTI capsules are available in white, induction-sealed, square, high-density polyethylene bottles with child-resistant closure.

[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: *Adequate*

Information request went on 07/25/2025:

The proposed USPI Section 16 lists (b) (4) 90-count packaging configuration, (b) (4) proposed in the application. (b) (4)

(b) (4)

Response received on 08/01/2025:

The Applicant plans to market (b) (4) 90-count packaging configuration. (b) (4)

(b) (4)

Assessment: *acceptable*

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)[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	Manufactured for Kura Oncology, Inc., San Diego, CA 92130 KOMZIFTI™ is a trademark of Kura Oncology, Inc.

Assessment: *Adequate*

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

(Provide any revision, if applicable, e.g., different color font, strikethrough, etc.) ***Any issues should be listed at the end in "OUTSTANDING ISSUES AND RECOMMENDATIONS"***

2.0 PATIENT LABELING

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

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[24]	Adequate	Ziftomenib is the United States Adopted Name (USAN).
Special preparation instructions (if applicable).	N/A	N/A
Storage and handling information (if applicable).	Adequate	The storage temperature should be listed in degree Celsius first, then in degree Fahrenheit between parentheses.
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differ from the dosage form.	N/A	No desiccant
Active ingredient(s) (if applicable).	Adequate	Ziftomenib is the only active ingredient in the drug product.
Alphabetical listing of inactive ingredients (if applicable).	Adequate	The Applicant should list the excipients in alphabetical order.
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Adequate	

Assessment: *Adequate*

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

3.0 CONTAINER AND CARTON LABELING[25]

3.1 Container Labels[26]

(b) (4)

3.2 Carton Labeling

The Applicant did not submit any carton labeling.

[25] Carton and Container Labeling Resources

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

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Proprietary name and established name[27], (font size and prominence) [§ 201.10(g)(2)].	Adequate	Choose an item.	Ziftomenib should be between parentheses.
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	Adequate	Choose an item.	
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	N/A	Choose an item.	
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>].	N/A	Choose an item.	
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	Adequate	Choose an item.	
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Adequate	Choose an item.	
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	Choose an item.	
Lot number and expiration date [§ 201.18 & 201.17].	Adequate	Choose an item.	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	Choose an item.	

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

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

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

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
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>).	N/A	Choose an item.	
Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5) or limited space per § 201.10(i)(2)].	N/A	Choose an item.	
For parenteral injectable dosage forms, include quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	Choose an item.	
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)].[30]	Adequate	Choose an item.	
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	Choose an item.	

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

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	Choose an item.	
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	Adequate	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>).	N/A	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.[31]	N/A	Choose an item.	
And others if space is available.	N/A	Choose an item.	

[31] USP General Notices 3.20 Indicating Conformance

Assessment of Carton Labels and Container Labeling: *Adequate*
Information request sent on 07/25/2025:
The drug name "ziftomenib" is not displayed in parentheses following the proprietary name "Komzifti" on the bottle labels, as proposed in the PI. Submit bottle label (b) (4) (b) (4) showing "Komzifti (ziftomenib) capsules" - with the drug name between parentheses. Refer to FDA 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) for further information.
Response received on 08/01/2025:
The Applicant plans to market only the 90-count packaging configuration. The bottle label for the 90-count packaging configuration has been updated showing the drug nonproprietary name in parentheses as follows: “Komzifti (ziftomenib) capsules”.
Assessment: *acceptable*
Response received on 08/21/2025:
The Applicant submitted an updated copy of the bottle label.
Assessment: *adequate*
The drug nonproprietary name is in parentheses as follows: “Komzifti (ziftomenib) capsules”

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

The container label and prescribing information comply with all regulatory requirements and are recommended for approval from a CMC perspective.

Primary Labeling Assessor Name and Date: Damien Y. Duveau, PhD, 09/15/2025

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

Damien Duveau

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David Claffey

Digitally signed by David Claffey
Date: 9/15/2025 02:43:32PM
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U.S. FOOD & DRUG ADMINISTRATION

CHAPTER VI: BIOPHARMACEUTICS

NDA Number	NDA 220305
Regulatory Pathway	505(b)(1)
Assessment Cycle Number	1
Drug Product Name/ Strength	Ziftomenib 200 mg capsules
Route of Administration	Oral
Applicant Name	Kura Oncology, Inc.
Proposed Indication	(b) (4)
Dosage and Administration	The recommended dosage of KOMZIFTI is 600 mg taken orally once daily until disease progression or unacceptable toxicity
Primary Reviewer	Alaadin Alayoubi, PhD.
Secondary Reviewer	Anitha Govada, PhD.

Assessment Recommendation: Adequate

From a Biopharmaceutics perspective, NDA 220305 for Ziftomenib 200 mg capsules is **Adequate** and recommended for **Approval**.

Background:

Kura Oncology, Inc. is seeking approval for New Drug Application (NDA) 220305-ORIG-1 for Ziftomenib 200 mg capsules via the 505(b)(1) regulatory pathway (Cover Letter) for the treatment of adults with relapsed or refractory (R/R) acute myeloid leukemia (AML) with a nucleophosmin 1 (NPM1) mutation.
Ziftomenib drug product is a 200-mg strength immediate-release (IR) Capsules with a proposed dosage of 600 mg (3 x 200 mg Capsules) once daily. The capsule is a white opaque size 00 HPMC capsule imprinted with ZIF 200, containing white to off-white powder. Ziftomenib is an NME (New Molecular Entity) and was designated as an orphan drug for the treatment of AML and the proposed drug product was granted Fast-Track Designation and Breakthrough Therapy Designation. The proprietary name, KOMZIFTI, was conditionally accepted by FDA on 16 January 2024.

Review Objective

This Biopharmaceutics Review focuses on evaluation of the in vitro dissolution method and acceptance criterion as a quality control (QC) test for the proposed drug product, Ziftomenib Capsules, 200 mg.

Assessment Summary

- **In Vitro Dissolution method and Acceptance criterion: Acceptable**

The proposed in vitro dissolution method and dissolution acceptance criterion shown in the table below were found acceptable for the Quality Control (QC) testing of Ziftomenib Capsules 200 mg, for batch release and stability testing (Proposed Dissolution method, page 4):

Apparatus	Speed	Medium and Temperature	Volume	Acceptance criterion
USP Apparatus II (Paddle)	60 rpm	0.01 N HCl, 37 °C	900 mL	Q = (b) (4) % in 45 minutes

Ziftomenib is a BCS Class II (low solubility/high permeability) drug substance. The Applicant has adequately justified the selection of 0.01 N HCl as the dissolution medium based on solubility studies demonstrating pH-dependent solubility, with adequate sink conditions achieved in acidic media and low solubility at neutral pH. The use of a paddle speed of 60 rpm with USP Apparatus II was supported by dissolution studies showing that higher speeds (e.g., 75 rpm) led to overly rapid dissolution, while lower speeds (50 rpm) resulted in incomplete release. The proposed method was shown to be capable of detecting differences in dissolution profiles due to variations in critical material and process attributes, including API particle size and (b) (4) parameters, and to a lesser extent, formulation variables such as (b) (4) content. All tested batches, including clinical and registration lots, achieved the proposed acceptance criterion of NLT (b) (4) % drug release in 45 minutes. The final method and acceptance criteria are considered adequate for quality control purposes. Additionally, the proposed to-be-marketed (commercial/registration) formulation is identical to the clinical formulation used in the pivotal BA/BE studies. Therefore, from a biopharmaceutics perspective, formulation bridging between the clinical and registration batches is not required.

List of Submissions Being Assessed:

SDN #	Date	Documents Assessed
1	03/31/2025	Original NDA Submission
6	05/23/2025	Updated Dissolution Method Development Report
11	06/23/2025	Information Request Response

Concise Description of Outstanding Issues (list bullet points with key information and update as needed):

None

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BIOPHARMACEUTICS ASSESSMENT

B.1 BCS DESIGNATION

Assessment: A BCS designation was neither requested nor needed

Solubility:

The Applicant provided solubility data for Ziftomenib API in various pH media (0.1 N HCl, 0.01N HCl, acetate buffer pH 4.5 and phosphate buffer pH 6.8 and pH 7.5) at 37°C in the absence and presence of different (b) (4) (b) (4)) as listed in **Tables 1, 2 &3.**

Ziftomenib exhibits pH-dependent solubility. It has high solubility in acidic conditions, with solubility above 10 mg/mL in 0.1N HCl (pH 1.0) and approximately 10 mg/mL in 0.01N HCl (pH 2.0). However, its solubility decreases significantly as pH increases. At pH 4.5, ziftomenib is slightly soluble with a solubility of about 0.2 mg/mL. It becomes practically insoluble at pH 6.8 and 7.5. (b) (4)

(b) (4)

Table 1: Solubility of Ziftomenib API in in different dissolution media at 37°C (b) (4)

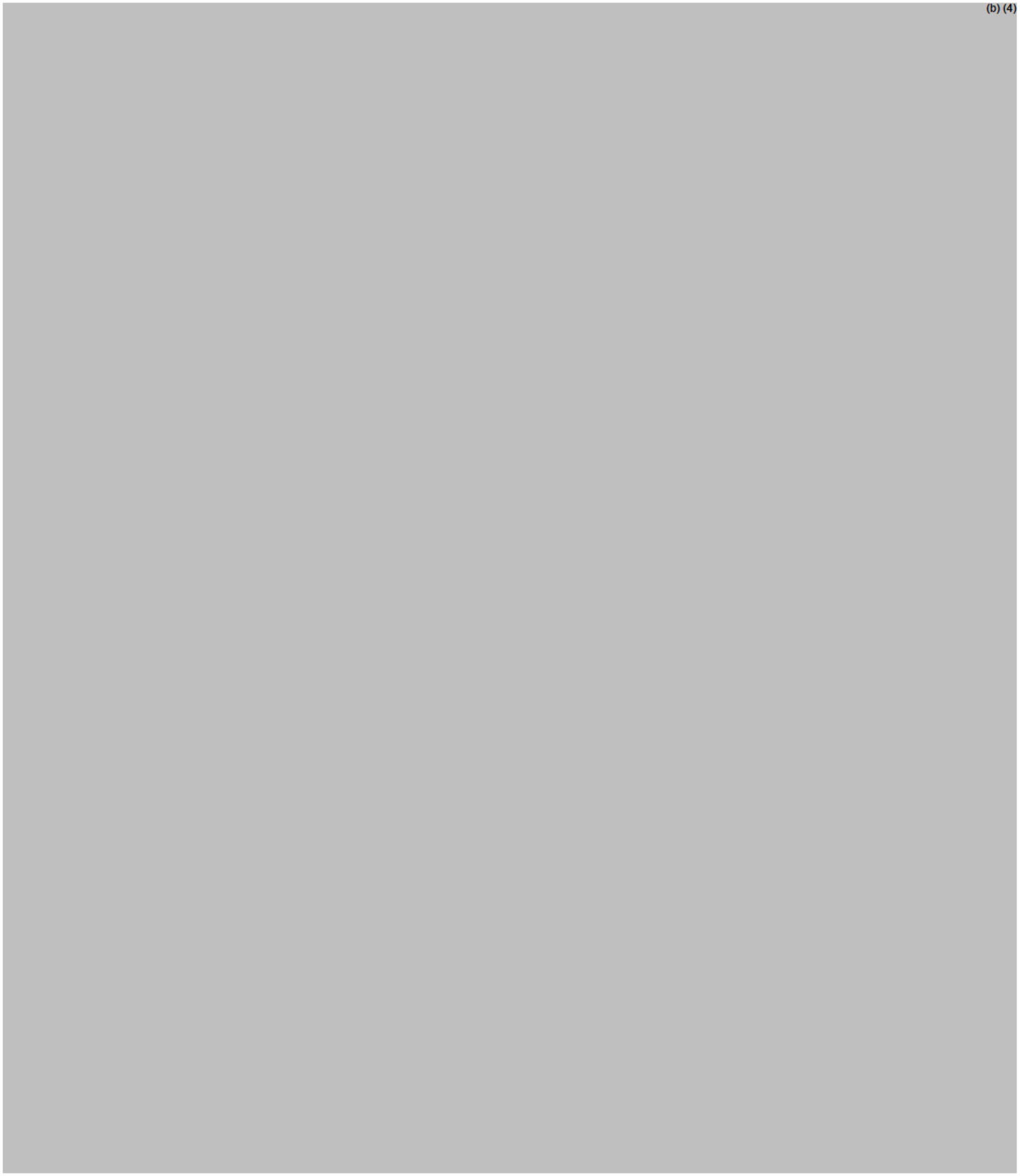
Target pH	Medium	Solubility (mg/mL)	pH before experiment	pH after experiment
1.0	0.1N HCl	> 10.07 a)	1.07	1.36
2.0	0.01N HCl	10.07	2.02	1.98 b)
4.5	50 mM Acetate Buffer, pH 4.5	0.21	4.53	4.64
6.8	50 mM Phosphate Buffer, pH 6.8	0.00	6.84	6.83
7.5	50 mM Phosphate Buffer, pH 7.5	0.00	7.51	7.52

a): Approximately 200 mg of ziftomenib API was added into 20 mL 0.1 N HCl, clear solution observed.

b): The pH was adjusted back to target 2.0 after addition of approximately 200 mg of ziftomenib API into 20 mL 0.01 N HCl due to significant pH increase from approximately pH 2 to approximately pH 4.

(b) (4)

(b) (4)



Reviewer's Assessment:

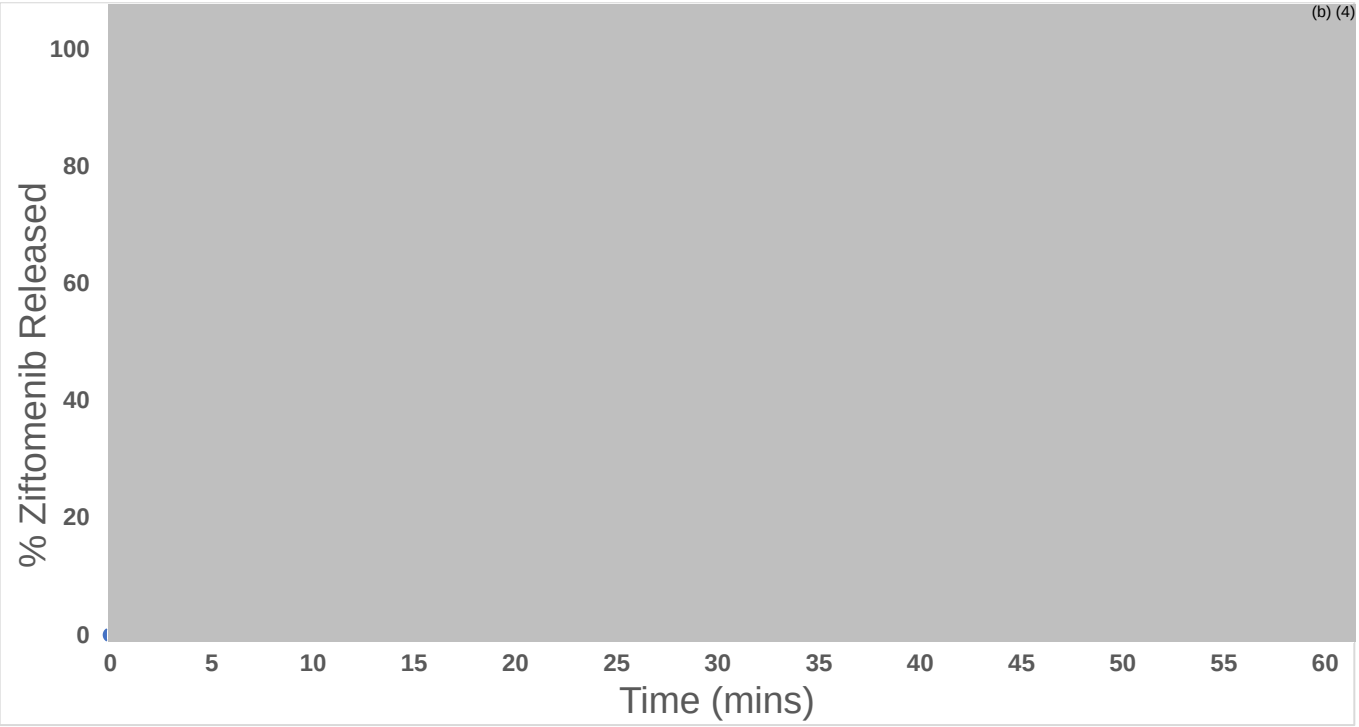
The submitted solubility data demonstrated that Ziftomenib is a pH-dependent drug substance, with

solubility decreasing as pH increases. Sink conditions (solubility > 0.67 mg/mL) were achieved in acidic media, but not in alkaline conditions. The submitted data indicate that Ziftomenib is a poorly soluble drug substance according to BCS criteria.

Permeability:
Ziftomenib demonstrated moderate permeability (permeability coefficient [A to B] = 2.69×10-6 cm/s) and was determined to be not a P-gp substrate in human colorectal adenocarcinoma (Caco-2) cells (efflux ratio=1.5, determined in the study KO-ADME-0037).

Dissolution:
Ziftomenib Capsules demonstrated complete and rapid dissolution, as shown for the representative registration stability batch (**CPYKG)** in **Figure 1**

Figure 1: Dissolution profile of representative registration stability batch (CPYKG) at 16 months (25°C/60% RH) for the proposed drug product Ziftomenib Capsules 200 mg using the proposed dissolution method.



B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA

Assessment: Adequate

(b) (4)

[redacted]

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(b) (4)

Based on the submitted data, Apparatus II with dissolution medium 0.01N HCl at 60 rpm paddle speed were selected as the optimal dissolution parameters.

Reviewer's Assessment:

Solubility studies demonstrated that Ziftomenib API exhibited the highest solubility in 0.01 N HCl, meeting sink conditions (b) (4) Based on these findings, the selection of 0.01 N HCl as the dissolution medium is considered acceptable.

During the IND-phase review of the dissolution method, the initially proposed paddle speed of (b) (4) rpm was deemed unacceptable (b) (4) . In alignment with this feedback, the Applicant proposed a paddle speed of 60 rpm in the submitted NDA, which was supported by data demonstrating reasonable dissolution profiles with relatively low variability. Although the Applicant did not formally evaluate different medium volumes, the selected volume of 900 mL was considered appropriate, as it ensured adequate sink conditions for the proposed drug product and is scientifically justified.

Evaluation of the discriminating ability of the proposed dissolution method:

To demonstrate the discriminating ability of the proposed dissolution method for Ziftomenib Capsules 200 mg, the Applicant conducted a series of studies evaluating the impact of formulation, process variables, and API particle size on the dissolution profile.

(b) (4)

(b) (4)

2

(b) (4)

Batch	Variable
(b) (4)	

(b) (4)

(b) (4)

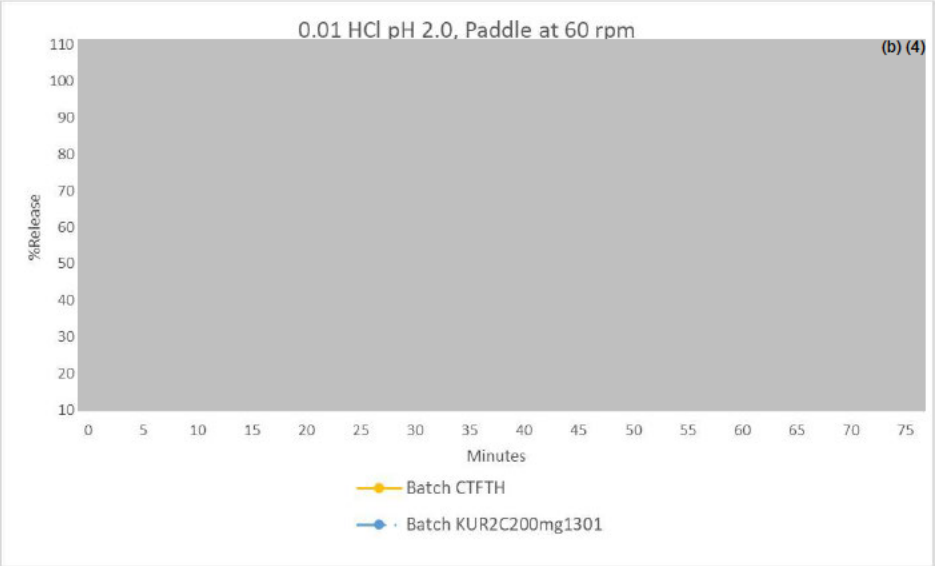
3. Effect of Drug substance Particle size on Dissolution:

The Applicant evaluated the impact of API particle size on dissolution by comparing the registration batch CTFTH, which had a (b) (4) particle size distribution (D10 (b) (4) µm, D50: (b) (4) µm, and D90: (b) (4) µm), with a small R&D batch, KUR2C200mg1301, which had a (b) (4) particle size distribution (D10 (b) (4) µm, D50: (b) (4) µm, and D90: (b) (4) µm) as listed in **Table 10**. Results showed that batch KUR2C200mg1301 exhibited a slower dissolution rate at early time points compared to the registration batch (CTFTH). Nonetheless, both batches achieved > (b) (4) % drug release by the 45-minute time point (**Figure 6**).

Table 10: Ziftomenib particle size distribution of the registration batch (CTFTH) and small R&D batch (KUR2C200mg1301).

Drug Product Batch	Drug Substance Batch / Manufacturer	Particle Size (µm)		
		D10	D50	D90
CTFTH (Registration Batch)	EF23001 / (b) (4)			(b) (4)
KUR2C200mg1301(Small R&D Batch)	452-24-01-60 / (b) (4) (b) (4)			

Figure 6: Dissolution profiles of Ziftomenib Capsules batches manufactured with variation of API particle size distribution.



Reviewer Assessment:

Given Ziftomenib's low solubility, API particle size is a critical factor that can significantly influence dissolution performance. The Applicant demonstrated that batches with larger particle size exhibited slower dissolution rates at early time points compared to those with smaller particle size. However, both batches met the proposed acceptance criterion of ≥ (b) (4)% drug release by 45 minutes. Nevertheless, the Applicant proposed to implement tight controls on the API particle size distribution. This control strategy is appropriate and should minimize the risk of batch-to-batch variability in dissolution behavior attributable to particle size differences.

Final Proposed dissolution method:

Based on the above studies, the Applicant proposed the following dissolution method for quality control purposes for release and stability of the proposed drug product Ziftomenib Capsules 200 mg:

Apparatus: USP Apparatus II (Paddle)

Medium: 900 mL of 0.01 N Hydrochloric Acid (HCl)

Paddle Speed: 60 rpm

Temperature: 37 ± 0.5°

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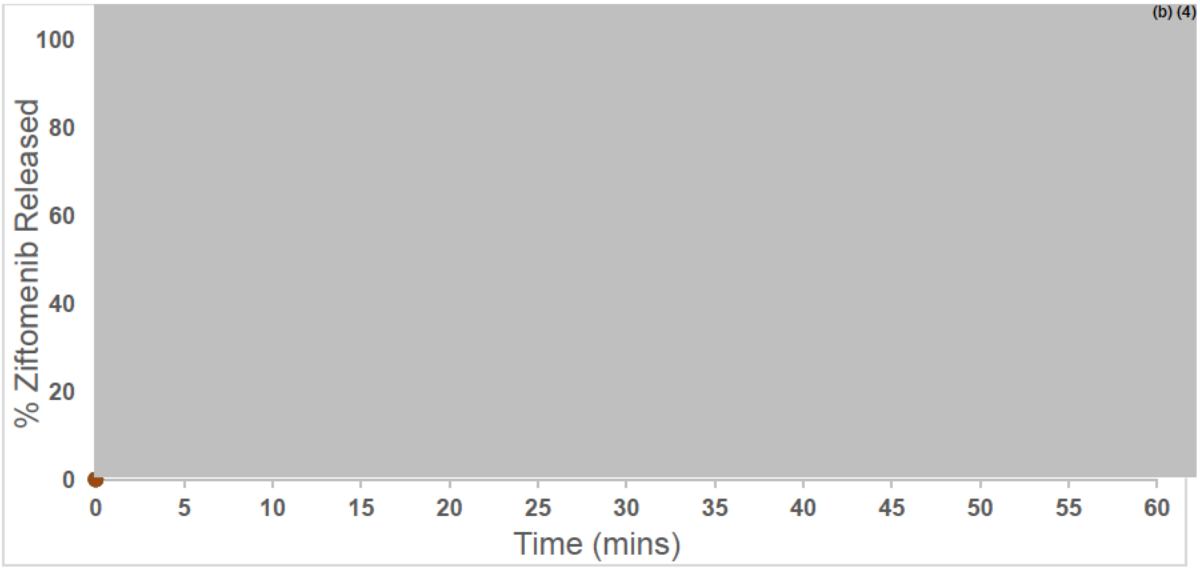
Overall Reviewer Assessment of the proposed dissolution method:

The proposed dissolution method for Ziftomenib Capsules 200 mg is considered acceptable based on the submitted data and overall justification. The Applicant has adequately supported the selection of 0.01 N HCl as the dissolution medium and 60 rpm as the paddle speed for USP Apparatus II. The discriminating ability of the method was evaluated in relation to several critical biopharmaceutical attributes (CBAs), including critical material attributes (CMAs), critical formulation variables (CFVs), and critical process parameters (CPPs). Specifically, the method was able to detect differences in dissolution behavior at early time points across batches with variations in API particle size, (b) (4) concentration, and (b) (4) conditions (e.g., (b) (4) Among these, (b) (4) and API particle size had the most pronounced effect on dissolution performance. Despite variability in early dissolution profiles, all batches achieved ≥ (b) (4)% drug release by 45 minutes. To mitigate potential batch-to-batch variability, the Applicant has proposed appropriate controls on API particle size.

Dissolution Data and Acceptance Criterion: Acceptable

The Applicant submitted complete dissolution data (individual, mean, range; RSD < 10%, n = 12 units) for the registration batches (CTFTH and CNGVH/ Data, pages 27 and 31) as well as for the registration stability batches (CPYKG, CPYKH , CPYKK , CPYKN , CPYKP and CPYKS/Data, page 29) at 16 months (25 °C/60% RH). The summary dissolution profiles demonstrated complete release at 60 minutes and >80% dissolution at 45 minutes, with high variability (RSD >10%) observed at early time points. Dissolution data are presented in **Figure 7**. Based on the submitted data, the Applicant initially proposed a dissolution acceptance criterion of NLT (b) (4)% in 45 minutes. This proposal was deemed inadequate, and in IR#1 (dated 06/16/2025), the Applicant was informed that the acceptance criterion should correspond to a point where at least Q = (b) (4)% dissolution is achieved. In their response (dated 06/23/2025), the Applicant agreed with the recommendation and revised the proposed dissolution specification to NLT (b) (4)% (Q) in 45 minutes. The Applicant acknowledged that this criterion may, at times, necessitate Stage 2 or Stage 3 testing.

Figure 7: Dissolution profiles of registration batches (CTFTH and CNGVH) and registration stability batches (CPYKG, CPYKH, CPYKK, CPYKN, CPYKP and CPYKS) of the proposed drug product at 16 months stability time point (25 C/ 60% RH) using the proposed dissolution method.



B.3. DRUG PRODUCT BRIDGING

Assessment: Adequate

Formulation Bridging: N/A

The proposed to-be-marketed/commercial/registration formulation is same as that of the clinical formulation (used in the Pivotal BA/BE Studies). Therefore, from a biopharmaceutics standpoint, formulation bridging is not required between the registration batches and the batches studied in the pivotal clinical trials.

B.4. BIOWAIVER REQUEST

Assessment: N/A

There was no request for biowaiver nor needed. The drug product is proposed to be marketed in one strength only, Ziftomenib Capsules, 200 mg.

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None

Appendix. Biopharmaceutics Information Requests

Biopharmaceutics Information Request #1 dated 06/16/2025:

We acknowledge receipt of your updated dissolution method development report (Sequence #0005, dated: 5/23/2025) in which you propose to use an in-house dissolution method [USP Apparatus II (Paddle), 900 mL of 0.01 N HCl, 60 rpm] for the proposed drug product Ziftomenib Capsules, 200 mg. Upon review, the proposed dissolution method is deemed adequate. However, the proposed dissolution acceptance criterion of "Q = (b)(4)% in 45 minutes" is considered too (b)(4) to ensure adequate quality control (QC) for the proposed drug product. In general, the selection of sampling timepoint for setting the acceptance criterion should be based on the dissolution data of the clinical/ registration batches, where NLT (b)(4)% (Q) dissolution occurs. Note that the dissolution acceptance criterion is set based on the n=12 data from clinical/ registration batches. Therefore, sometimes stage 2 testing and occasionally stage 3 testing may be needed. If dissolution failures are observed on stability, then these failures should be described. Discuss any corrective actions to avert such dissolution failures and provide a new batch data to demonstrate correction of the issue, if needed.

Implement the recommended acceptance criterion for your drug product at both release and stability and update the drug product release and stability specifications with the revised acceptance criterion for the dissolution test accordingly.

Link to the Applicant's Response dated 06/23/25:
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Primary Biopharmaceutics Assessor's Name and Date:

***Alaadin Alayoubi**, Ph.D. (07/28/2025)*

Secondary Assessor Name and Date:

***Anitha Govada,** Ph.D. (07/28/2025)*

Alaadin Alayoubi

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Anitha Palamakula Govada

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