CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218436Orig1s000

PRODUCT QUALITY REVIEW(S)

Office of Pharmaceutical Quality

New Drug Application (NDA) 218436
Integrated Quality Assessment

RECOMMENDATION

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

NDA 218436
Assessment #1

Drug Product Name	Remibrutinib
Dosage Form	Tablets
Strength	25 mg/tablet
Route of Administration	oral
Rx/OTC Dispensed	Rx
Applicant	Novartis Pharmaceuticals Corporation
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original (SD-1)	31-Jan-2025	All
Amendment (SD-8)	27-Mar-2025	Drug product
Amendment (SD-12)	30-Apr-2025	Drug product
Amendment (SD-17)	28-May-2025	Manufacturing/facilities
Amendment (SD-18)	30-May-2025	Drug product
Amendment (SD-22)	05-Jun-2025	Manufacturing/facilities
Amendment (SD-23)	05-Jun-2025	Drug substance
Amendment (SD-27)	07-Jul-2025	Manufacturing/facilities
Amendment (SD-28)	15-Jul-2025	Manufacturing/facilities
Amendment (SD-29)	18-Jul-2025	Drug Product[1]
Amendment (SD-31)	24-Jul-2025	Manufacturing/facilities

[1] Note that the updated stability data (an additional 9 month time-point 25°C/60%RH) provided in the SD-29 amendment on 18-Jul-2025 for the three supportive batches 1010063750m 1010064143, and 1010064144, did not change the decision to grant the 24 month shelf-life as per the drug product chapter finalized just before the Quality Due Date of 30-Jun-2025.

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Zhixing Shan	Donna Christner
Drug Product	Afsana Tajmim	Craig M. Bertha
Manufacturing	Jing Fang Established Conditions (ECs): Eric A. Twum/Geok Yan Loo	Jean Tang ECs: Marcus F. Yambot
Microbiology	Jing Fang	Jean Tang
Biopharmaceutics	Swapna Pamu	Tapash Ghosh
Labeling	Afsana Tajmim	Julia Pinto
Regulatory Business Process Manager	Emma Gimose	
Application Technical Lead	Craig M. Bertha	
Laboratory (OTR)	N/A	
Environmental	Xiaoqin Wu	

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QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	Type III	(b) (4)		N/A		Adequate information in NDA
	Type III			N/A		Adequate information in NDA
	Type III			N/A		Adequate information in NDA
	Type III			N/A		Adequate information in NDA
	Type III			N/A		Adequate information in NDA

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

Document	Application Number	Description
IND	131325	For chronic spontaneous urticaria
IND		(b) (4)
IND		
IND		

2. CONSULTS

Disciplines	Status	Recommendation	Date	Assessors
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH	N/A			
Clinical	N/A			
Statistical (see appendix)	Complete	Acceptable	19-May-2025	Marcus Migura & Yingjie Wang

Office of Pharmaceutical Quality

New Drug Application (NDA) 218436
Integrated Quality Assessment

NDA Executive Summary

1. Application/Product Information

NDA Number	218436		
Applicant Name	Novartis Pharmaceuticals Corporation		
Drug Product Name	Remibrutinib tablets		
Dosage Form	Tablet		
Proposed Strength(s)	25 mg/tablet		
NDA Classification	Type 1 - NME		
Route of Administration	Oral		
Maximum Daily Dose	50 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	Chronic spontaneous urticaria (CSU)		
Drug Product Description	Film coated tablets – Shape: round, curved without score; color: light yellow; imprint: Debossed LV on one side, Novartis symbol (b) (4) on the other side		
Co-packaged product information	N/A		
Device information	N/A		
Storage Temperature/ Conditions	Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°-30°C (59°-86°F) [see USP Controlled Room Temperature]. Store in the original packaging in order to protect from moisture.		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Zhixing Shan	Donna Christner
	Drug Product/ Labeling	Afsana Tajmim	Craig M. Bertha/Julia Pinto
	Manufacturing	Jing Fang	Jean Tang

	Biopharmaceutics	Swapna Pamu	Tapash Ghosh
	Microbiology	Jing Fang	Jean Tang
	Established Conditions (ECs):	Eric A. Twum/Geok Yan Loo	Marcus F. Yambot
	RBPM	Emma Gimose	
	ATL	Craig M. Bertha	
Consults	*Environmental Assessment* – Xiaoqin Wu		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: 24 month

b. Additional Comments for Action N/A

4. Basis for Recommendation:

a. **Summary of Rationale for Recommendation:** The applicant has provided additional information in response to Agency information requests and there are no unresolved CMC-related issues remaining. Therefore, approval of the application is recommended from the CMC perspective.

b. **Is the overall recommendation in agreement with the individual discipline recommendations?** Choose an item.

Recommendation by Subdiscipline:

Drug Substance - Adequate
Drug Product - Adequate
Quality Labeling - Pending[1]
Manufacturing - Adequate
Biopharmaceutics - Adequate
Microbiology - N/A

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

[1]The labeling review decision is pending for this IQA due to ongoing negotiations with the applicant. There are only minor labeling deficiencies from the CMC perspective and we expect the applicant will accept our recommendations. Refer to the CMC sections of the final approved labeling.

5. Life-Cycle Considerations

Established Conditions per ICH Q12: Yes

Comments: Refer to the chapter entitled *Pharmaceutical Quality System Assessment for Established Conditions*

Comparability Protocols (PACMP): Yes

Comments: Refer to the chapter entitled *Pharmaceutical Quality System Assessment for Established Conditions*

Additional Lifecycle Comments: N/A

Application Technical Lead Name and Date:

Craig M. Bertha, CMC Reviewer, 30-Jul-2025

Final Risk Assessment for NDA 218436

DP CQA	Factors that may impact the CQA	O[2]	S[1, 3]	D[1]	Comment & considerations for risk assessment	Final RA	Lifecycle considerations
Appearance	▪Film coating (b) (4) variation ▪Legibility of debossing ▪Friability problems with (b) (4) cores	2	3	3	(b) (4)	18	
Identity	▪API solid state variation ▪API solid state change during manufacture (e.g., (b) (4)) ▪API solid state change during shelf life of drug product	1	3	5		15	
Assay	▪Incorrect amount of API formulated ▪API degradation during manufacture and during shelf-life	2	3	3		18	
Degradation Products	▪High degradant levels in input API ▪API/excipient compatibility issues	2	3	3		18	

[2] O = Probability of Occurrence; S = Severity of Effect; D = Detectability
[3] Severity of effect can only be estimated; input from clinical, clinical pharmacology, and pharmacology/toxicology team would be necessary for more accurate assessment of clinical impact of failures of product CQAs (thus a median value of "3" will be used throughout)

	▪Degradation of API during manufacture and during shelf-life				(b) (4)		
Dissolution	▪Solid state variation of API prior to formulation ▪Solid state conversion of API as formulated ▪Variation in input API particle size distribution (PSD) ▪Process parameter variations	2	3	3		18	
Uniformity of Dosage Units (content uniformity or CU)	▪Process parameter variations for (b) (4) (b) (4)	2	3	2		12	
Particle size (photon correlation spectroscopy)		2	3	1		6	
(b) (4)	(b) (4)	2	3	1		6	

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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	218436
Assessment Cycle Number	1
Drug Product Name	Tradename (remibrutinib) tablet

Assessment Recommendation: Choose an item.

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

Brief Description of Outstanding Issues:

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
0000, SDN#1	01/31/2025	Original-1

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

Submitted on January 31, 2025, SDN#1

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

[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)

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights[2] [21 CFR 201.57(a)(2)]		
Established name(s)[3]	Adequate	
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]	N/A	
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]	N/A	

Assessment: *Adequate*

1.2 FULL PRESCRIBING INFORMATION

(b) (4)

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

[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)

[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

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)
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	
For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11]	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.*[x]*"* with x numerical citation to "OSHA Hazardous Drugs."	N/A	

Assessment: *Adequate*

[11] §201.57(c)(3)(iv)
[12] USP General Notices 2.30 Legal Recognition

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.	N/A	
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 criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	

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

Assessment: *Adequate*

1.2.3 Section 11 (DESCRIPTION)[14]

(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	
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:	N/A	

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

[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)
"TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg 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	
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	Defer to Pharm-tox team.
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Inadequate	Chemical name is not included.

[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)
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)].	Inadequate	Drug substance's description and solubility profile should be included, as follows- "Remiburtinib is a crystalline or amophorous solid, soluble in water, insoluble in alcohol".
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").	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	

Assessment: *Inadequate*

- Chemical name should be added in section 11.
- Drug substance's description and solubility profile should be included, as follows-

"Remiburtinib is a crystalline or amophorous solid, soluble in water, insoluble in alcohol".

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

(b) (4)

[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)].	Inadequate	Dosage form should be added.
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.	Inadequate	Strength should be added.
Available units (e.g., bottles of 100 tablets) [§ 201.57©(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©(17)(iii)].	Inadequate	Tablet description should be included.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state “functionally scored.”	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	

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©(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).	Adequate	

[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*

- Dosage form and strength should be added in section 16.
- Identification of dosage forms should be included as follows:
  "Tablet description: light yellow, round, curved, unscored, film-coated tablet, debossed with "LV" on one side and "Novartis" logo on the other side. Tablet diameter is 7 mm".

1.2.5 Other Sections of Labeling

N/A

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.	Inadequate	Manufacturer's information should be included. Street address of distributor should be added.

Assessment: *Inadequate*

- Manufacturer's information should be included.
- Street address of distributor should be added.

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	
Special preparation instructions (if applicable).	N/A	

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

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Storage and handling information (if applicable).	Adequate	
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.	Adequate	
Active ingredient(s) (if applicable).	Adequate	
Alphabetical listing of inactive ingredients (if applicable).	Adequate	
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Inadequate	Manufacturer's information should be included. Street address of distributor should be added.

Assessment: *Inadequate*

- Manufacturer's information and street address of distributor should be included per the labeling review tool.

3.0 CONTAINER AND CARTON LABELING[25]

[25] Carton and Container Labeling Resources

3.1 Container and Cartoon Labels[26]

(b) (4)

[redacted]

[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	Yes	
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	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>].	N/A	N/A	
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	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].	Inadequate	Yes	Lot number and expiration date is not displayed in the carton's label.
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	Yes	

[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	N/A	
Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5) or limited space per § 201.10(i)(2)].	N/A	Yes	
For parenteral injectable dosage forms, include quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	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	
Linear Bar code [§ 201.25(c)(2)].[30]	Adequate	Yes	
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	Yes	

[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)].	Inadequate	Yes	"Product of China" sentence is confusing as the drug product is manufactured in Novartis d.o.o., Ljubljana, 1000, Slovenia, and (b) (4) Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936.
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	Adequate	Yes	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	Yes	
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	N/A	Yes	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	N/A	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference	N/A	Yes	

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)
shall be plainly stated on its label.[31]			
And others if space is available.	N/A	N/A	

Assessment of Carton Labels and Container Labeling: *Inadequate*

- Lot number and expiration date should be included in the carton's label.
- The carton's label contains a critical discrepancy where the product is stated to be manufactured by Novartis d.o.o., Ljubljana, 1000, Slovenia and (b) (4) Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936, yet displays "Product of China" below this information, creating conflicting country of origin statements that must be corrected to ensure regulatory compliance and accurate representation of the drug product's actual manufacturing location.

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

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 issues in this section.

Full Describing Information

Section 11 (Description):

- *Chemical name should be added in section 11.*
- *Drug substance's description and solubility profile should be included, as follows- "Remiburtinib is a crystalline or amophorous solid, soluble in water, insoluble in alcohol".*

Section 16 (How supplied/storage and handling):

- *Dosage form and strength should be added in section 16.*

[31] USP General Notices 3.20 Indicating Conformance

- *Identification of dosage forms should be included as follows:*
- *"Tablet description: light yellow, round, curved, unscored, film-coated tablet, debossed with "LV" on one side and "Novartis" logo on the other side. Tablet diameter is 7 mm".*

Manufacturing Information After Section 17 (for drug products):

- *Manufacturer's information and street address of distributor should be included per labeling review tool.*

Patient Labeling

- *Manufacturer's information and street address of distributor should be included per labeling review tool.*

Container Labels and Carton Labeling

- *Lot number and expiration date should be included in the carton's label.*
- *The carton's label contains a critical discrepancy where the product is stated to be manufactured by Novartis d.o.o., Ljubljana, 1000, Slovenia and* (b) (4) *Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936, yet displays "Product of China" below this information, creating conflicting country of origin statements that must be corrected to ensure regulatory compliance and accurate representation of the drug product's actual manufacturing location*.

Primary Labeling Assessor Name and Date:

Afsana Tajmim, Ph.D.
OPQ/OPQA II/Division VII
Secondary Assessor Name and Date (and Secondary Summary, as needed):
Julia Pinto, Ph.D.
OPQ/OPQA II/Division VIII

Afsana Tajmim

Digitally signed by Afsana Tajmim
Date: 7/08/2025 01:12:06PM
GUID: 631a6fb900acee59d61c3d8140d343db

Julia Pinto

Digitally signed by Julia Pinto
Date: 7/08/2025 01:56:32PM
GUID: 5050dbcb00001294a888a4bdc20a3a58

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CHAPTER VI: BIOPHARMACEUTICS

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

NDA Number	NDA-218436-ORIG-1
Assessment Cycle Number	1
Drug Product Name/ Strength	Remibrutinib film-coated tablet, 25 MG
Route of Administration	Oral
Applicant Name	Novartis Pharmaceuticals Corporation
Therapeutic Classification/ OND Division	Division of Pulmonology, Allergy, and Critical Care (DPACC)
LD Number	NA, this is an NME
Proposed Indication	Treatment of chronic spontaneous urticaria in adult patients who remain symptomatic despite H1-antihistamine treatment.

Assessment Recommendation: **Adequate**

A. Assessment Summary:

The Applicant is seeking approval for the proposed drug product remibrutinib film coated tablets, 25 mg via 505(b)(1) pathway. It is an immediate release dosage form for oral administration. It is indicated for the treatment of chronic spontaneous urticaria (CSU) in adult patients who remain symptomatic despite H1-antihistamine treatment. The clinical development of remibrutinib for CSU has been conducted under IND 131325. The Applicant is requesting priority review.

Remibrutinib is a new molecular entity (NME) and it is the free form of a weak base showing high permeability and low solubility at physiological pH (BCS Class 2). Applicant developed 25 mg, 50 mg and 100 mg strengths but this NDA only includes the 25 mg strength. All strengths have formulation proportionality, see appendix 1 for formulation details.

The Applicant requested to approve Rhapsido as the proprietary name for the proposed drug product on May 15, 2023, under IND 131325[1] and it was conditionally approved by the Agency on 10/31/2023[2].

There is no dissolution method listed in FDA dissolution methods database or USP monograph. Applicant developed an in-house method (Apparatus 1/ basket with 900 mL of 0.1N hydrochloric acid, at 100 rpm, 37 ± 0.5 °C) and provided dissolution method development data and discriminating ability data.

[1] \\CDSESUB1\EVSPROD\nda218436\0000\m1\us\cover-attachment2.pdf
[2] \\CDSESUB1\EVSPROD\nda218436\0000\m1\us\proprietary-names.pdf

The proposed dissolution acceptance criterion is Q= (b)(4)% in 20 minutes. Based on the provided dissolution data in QC media, all exhibit batches comply to the proposed acceptance criterion. The proposed dissolution method and acceptance criterion are acceptable from Biopharmaceutics perspective.

Table 1: Proposed dissolution method and acceptance criterion:

USP Apparatus	Speed (RPM)	Medium	Volume/Temp	Acceptance Criterion
I (Basket)	100	0.1N Hydrochloric acid (pH 1.2)	900 mL/37°C	Q = (b)(4)% at 20 minutes

The Biopharmaceutics review is focused on evaluation of (1) the adequacy of the proposed dissolution method and acceptance criterion and biopharmaceutics risk assessment.

Reviewer's Assessment:

I. Dissolution Method and Acceptance Criterion

Remibrutinib is a new molecular entity (NME) and belongs to BCS class 2 (low solubility and high permeability). There is no dissolution method listed in FDA dissolution methods database or USP monograph. Based on the solubility data provided by the Applicant, solubility in aqueous media is strongly pH dependent with high solubility in acidic media and very poor solubility in media at pH 3 and above. Therefore, remibrutinib is not considered highly soluble (BCS class 2).

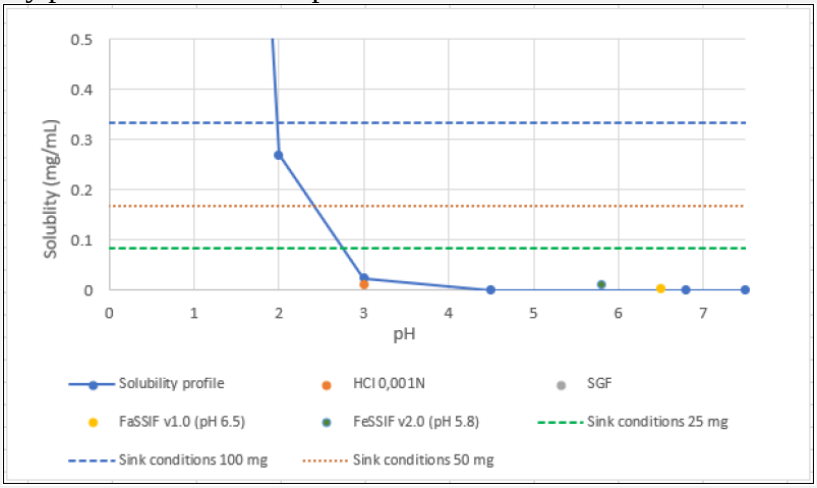
Table 2: Solubility data in different dissolution media at 37.0 ± 1.0 °C:

Medium	Solubility of remibrutinib
	Data reported (mg/mL)
Water	0.0000
FaSSIF v1.0	0.0041
FeSSIF v2.0	0.0121
SGF without enzyme[1]	2.3703
pH 1.2 (HCl 0.1N)	3.1995
pH 2.0 (HCl 0.01N)	0.2692
pH 3.0 (HCl 0.001N)	0.0109
Buffer pH 3.0 (citrate USP buffer)	0.0230
Buffer pH 4.5 (acetate USP buffer)	0.0000
Buffer pH 6.8 (phosphate USP buffer)	0.0000
Buffer pH 7.5 (phosphate USP buffer)	0.0000

[1] Buffer pH 1.2 (SGF without enzyme, 0.1N HCl/NaCl)

[2] Equilibrium solubility determined at 37°C ± 1°C after 24 hours.

Figure 1: Solubility profile of in various pH media at 37 °C - 900 mL



For a dissolution volume of 900 mL, the concentration of drug substance to achieve sink conditions corresponds to 0.083 mg/mL for the 25 mg dosage strength.

Applicant provided the dissolution method development and discriminating ability data[3].

Dissolution method development data[4]:

(b) (4)

[redacted]

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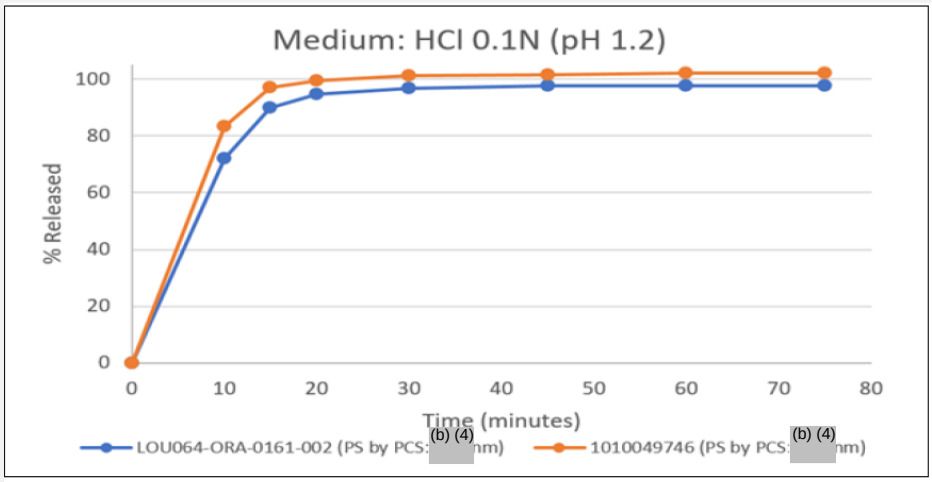
[4] \\CDSESUB1\EVSPROD\nda218436\0000\m3\32-body-data\32p-drug-prod\lou064-fct\32p2-pharm-dev\pharmaceutical-development-formulationdevelopment-mdr.pdf

Discriminating ability data:
The discriminating ability of the proposed dissolution method has been assessed on selected CBA (critical bioavailability attributes) which includes critical formulation variables (CFV), critical material attributes (CMA), critical process parameters (CPP).

1. Critical material variables: particle size distribution (PSD)

(b) (4)

Figure 4: Dissolution profiles of 25 mg with different PSD in 0.1N HCl:



Note: n=12 for batch 1010049746 and n=6 for LOU064-ORA-0161-002.

The dissolution method in 0.1N HCl showed no discrimination regarding the particle size of the drug substance in the (b) (4) range.

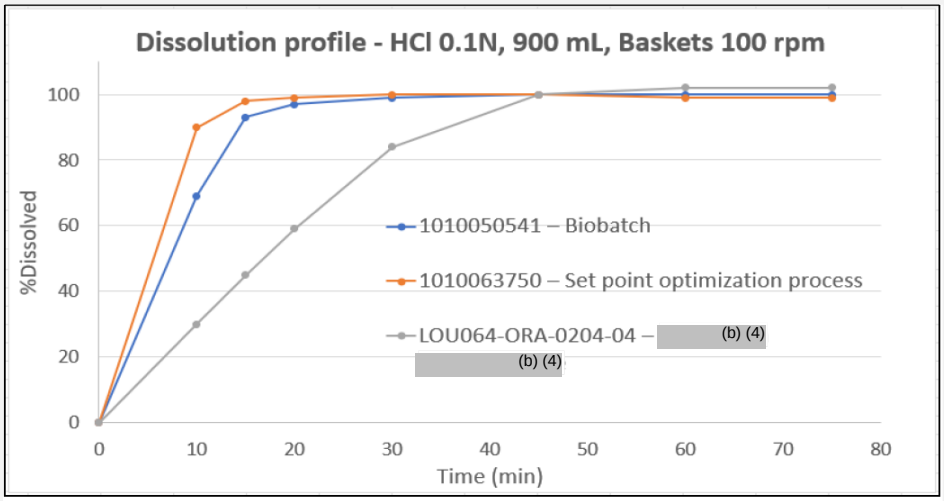
2. Critical formulation attributes: (b) (4):
The (b) (4) plays a crucial role in tablet formulation as it facilitates the (b) (4) (b) (4) and dissolution when exposed to dissolution media.

Compared to conventional formulations, where (b) (4) within a range of (b) (4)%, according to Handbook of Pharmaceutical Excipients, American Pharmaceutical Association (2003), the remibrutinib 25 mg tablet cores contain (b) (4) (b) (4). This (b) (4) in the formulation promotes the (b) (4)

To demonstrate the importance of (b) (4) in the formulation, a

prototype was manufactured using a low but still acceptable amount of (b) (4) (b) (4) of the total formulation, compensated with the (b) (4) (b) (4) The comparison of dissolution profiles from this prototype batch, the biobatch and the set point batch of the optimized process illustrates the influence of the (b) (4) level on the release rate of remibrutinib from the film-coated tablet. It demonstrates the discriminatory nature of the QC dissolution method, as a batch with prolonged (b) (4) time would be rejected, if the proposed criterion of Q = (b) (4)% at 20 minutes is applied.

Figure 5: Dissolution profiles of 25 mg containing drug substance with different concentration of (b) (4) using the proposed QC dissolution method**.**

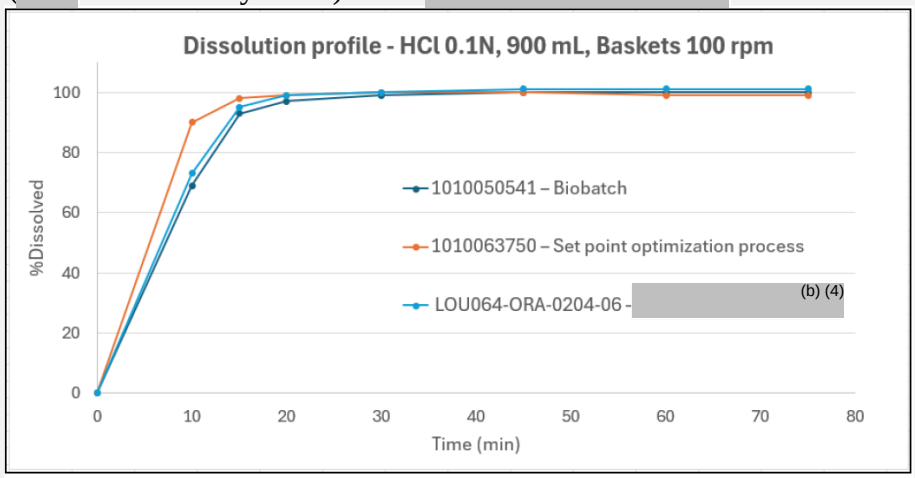


Note: n=6 for batch LOU064-ORA-0204-04 and n=12 for the other two batches.

3. Critical formulation attributes: (b) (4) (b) (4) (b) (4) were evaluated during the development of remibrutinib 25 mg film-coated tablets.

For the purposes of (b) (4) evaluation, three batches were compared, with the only variation being the (b) (4) used (batches 1010050541 and 1010063750 containing (b) (4), and batch LOU064-ORA-0204-06 containing (b) (4)). No physicochemical differences were observed between the batches containing either (b) (4) during the compatibility study. Furthermore, the dissolution performance, evaluated using the proposed QC dissolution method, showed minimal difference in the release of remibrutinib at the initial timepoint from the film-coated tablet when (b) (4) was used as (b) (4) instead of (b) (4).

Figure 6: Dissolution profiles of 25 mg containing drug substance with (b) (4) (b) (4) ((b) (4) confirmatory batch) and a (b) (4).



Note: n=6 for batch LOU064-ORA-0204-06 and n=12 for the other two batches

4. Critical process parameters: (b) (4).
The variables that may affect the performance of the film-coated tablets were selected based on a risk assessment of the manufacturing process. These variables include: (b) (4) (b) (4) (b) (4)

The (b) (4) step is essential for achieving the desired particle size of the drug substance, while the (b) (4) step is crucial for ensuring proper (b) (4) and (b) (4).

A proven acceptable range (PAR) was defined during manufacturing of the confirmatory batches. The manufacturing strategy for the confirmatory batches was defined to establish a range in process parameters at the '(-) Minus' level, '(+) Plus' level and '(SP) Set-Point' level for (b) (4) process steps. The parameters in the 'Minus' batch group led to (b) (4) and (b) (4) drug substance (b) (4) whereas the parameters in the 'Plus' group yielded (b) (4) and relatively smaller drug substance (b) (4)

5. Critical process parameters: Hardness
Sample cores collected from the (b) (4) step at different ratios of (b) (4) and hardness were used for the evaluation by using the finalized QC method.

Figure 7: Dissolution profiles for remibrutinib 25 mg FCT (film coated tablet) **Minus batch** at 0.1N HCl and pH 3 using (b) (4) at two different hardness ((b) (4) **N)** – Batch 1010050541

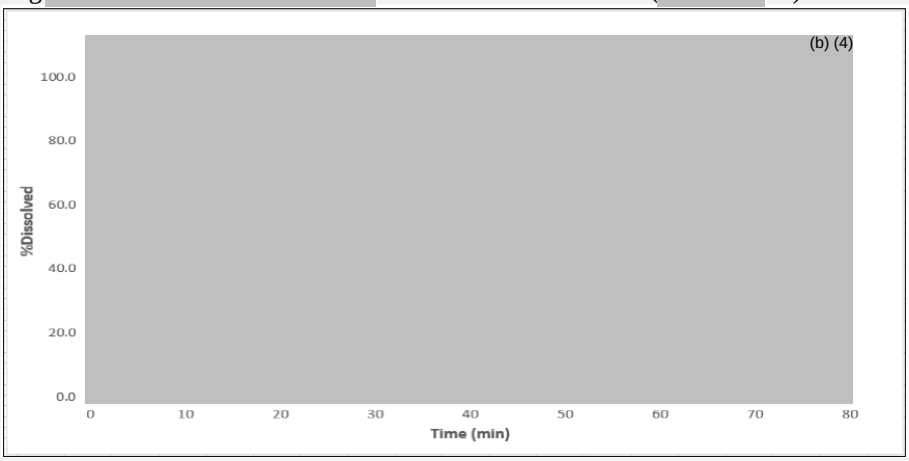


Figure 8: Dissolution profiles for remibrutinib 25 mg FCT **Minus batch** at 0.1N HCl and pH 3 using (b) (4), at two different hardness ((b) (4) **N)** – Batch 1010050541

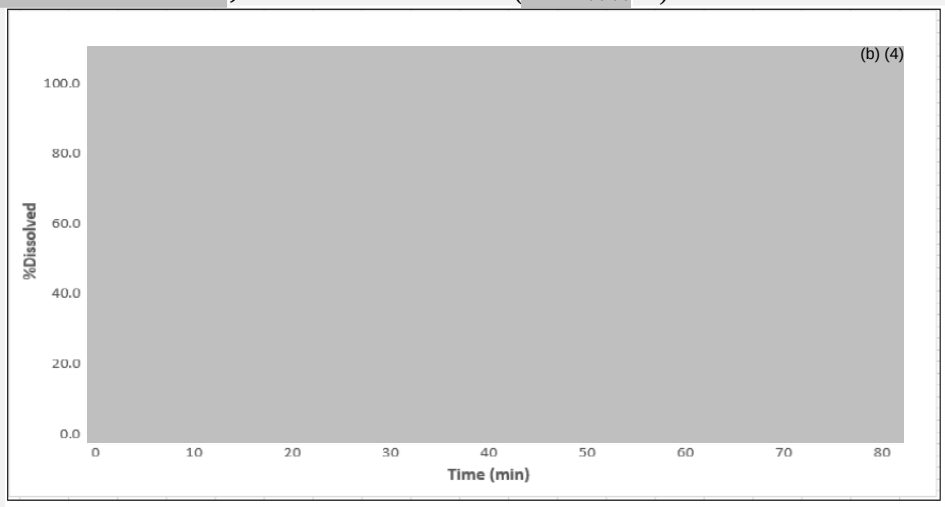


Figure 9: Dissolution profiles for remibrutinib 25 mg FCT **Set-Point** batch at 0.1N HCl and pH 3 using (b) (4) at two different hardness **(** (b) (4) **N)** – Batch 1010050542

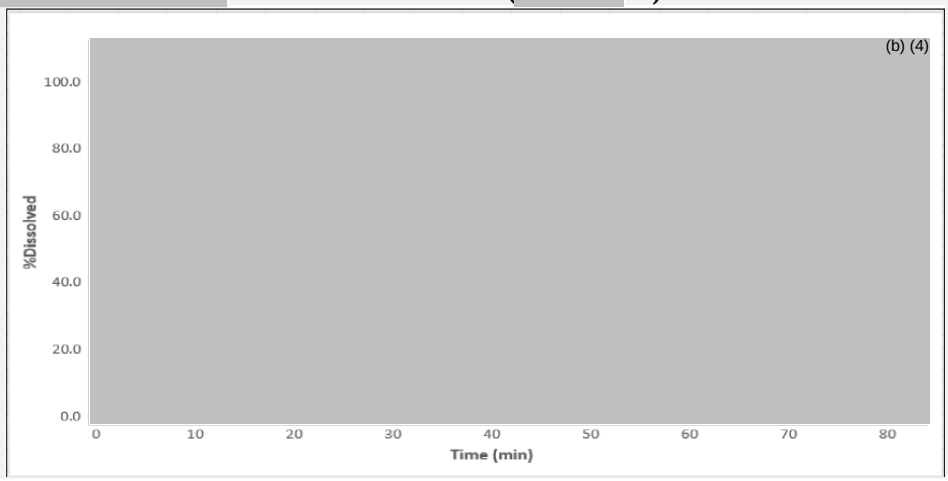


Figure 10: Dissolution profiles for remibrutinib 25 mg FCT **Set-Point** batch at pH 1.2 and pH 3 using (b) (4) at two different hardness ((b) (4) **N**) – Batch 1010050542

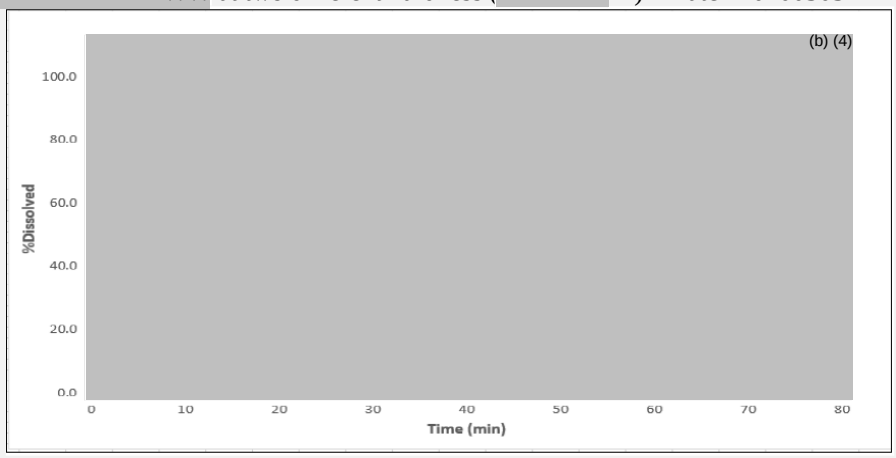


Figure 11: Dissolution profiles for remibrutinib 25 mg FCT **Plus batch** at 0.1N HCl and pH 3 using (b) (4) (b) (4) at two different hardness ((b) (4) **N**) – Batch 1010050543

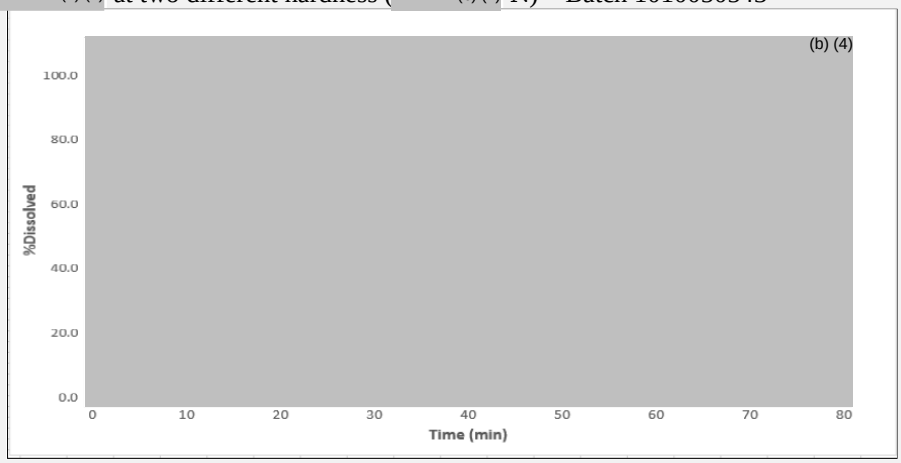
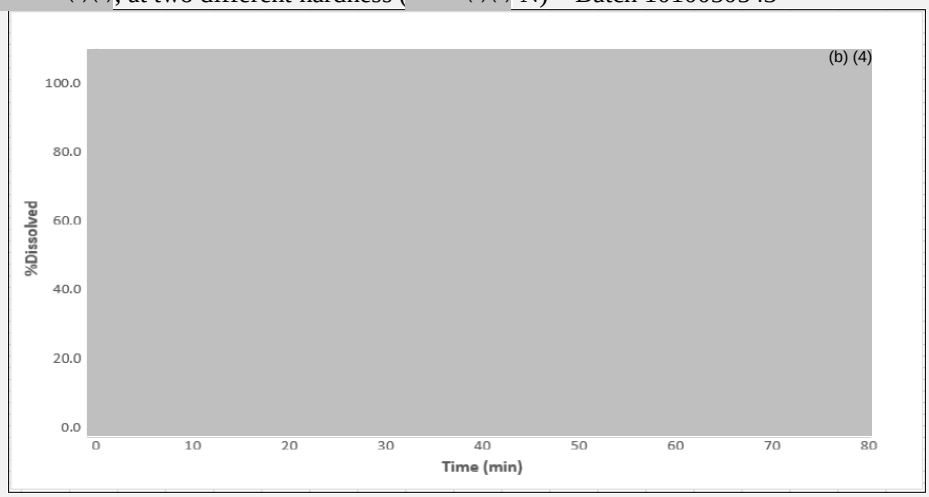


Figure 12: Dissolution profiles for remibrutinib 25 mg FCT Plus batch at 0.1N HCl and pH 3 using (b) (4) (b) (4), at two different hardness ((b) (4) N) – Batch 1010050543



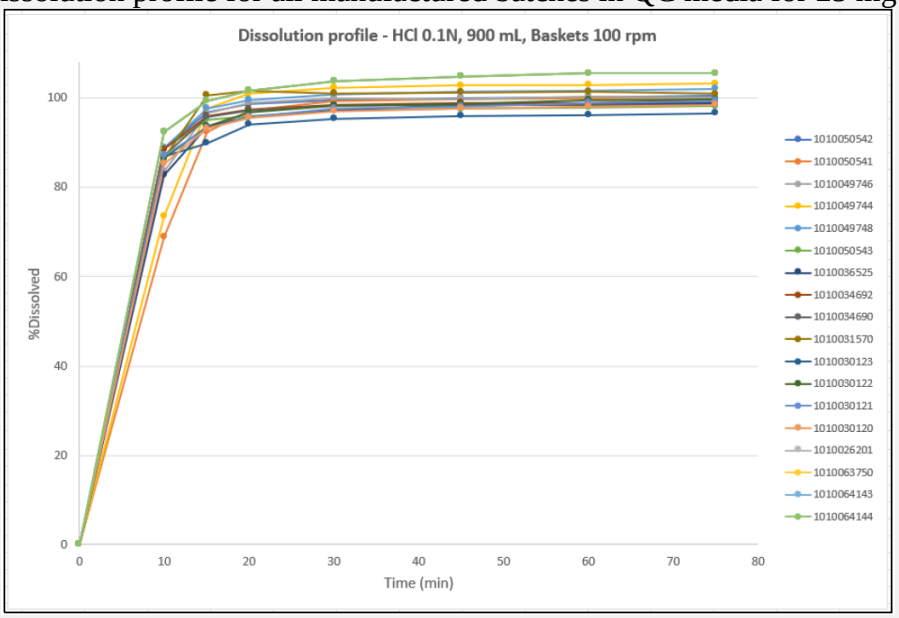
No significant impact of (b) (4) and tablet hardness was demonstrated in any of the

three batches that defined the manufacturing "safe space".

Based on the provided method development (where Applicant provided reasoning for the selection of dissolution medium, dissolution equipment and agitation speed) and discriminating ability data (which includes comparison of the target batch and aberrant batches with different PSD, amounts of (b) (4) and tablet hardness), it can be concluded that the proposed method (listed in table 1 above) is suitable for this test product.

Applicant provided dissolution data utilizing the QC method for more than 20 batches of the 25 mg and dissolution profile data is presented below in figure 4 (see Appendix 2 for individual unit dissolution data). Based on the submitted dissolution data, drug release is rapid with >80% in 15 minutes. Therefore, the proposed dissolution acceptance criterion of Q= (b) (4)% in 20 minutes is reasonable.

Figure 13: Dissolution profile for all manufactured batches in QC media for 25 mg:



II. Formulation Bridging:

Hard gelatin capsule strengths 0.5 mg, 5 mg, 20 mg, and 50 mg were used to support phase 1 clinical studies. In support of phase 2 clinical studies, additional strengths 10 mg and 25 mg were developed. The qualitative composition of the additional strengths was same as the strengths used in phase 1 clinical studies. During further development, (b) (4) was optimized, leading to a slight change in the amount of (b) (4) The optimized formulation is referred as formulation B but original and optimized formulations have the same qualitative composition and manufacturing process and differ in the quantitative composition only.

Though hard gelatin capsules were used to support phase 1 clinical studies, to enhance patient convenience with possible smaller dose units for the higher strengths and to (b) (4) a film-coated tablet (currently proposed product in this NDA) was developed for phase 2 and phase 3 clinical studies and later for commercialization. Film-coated

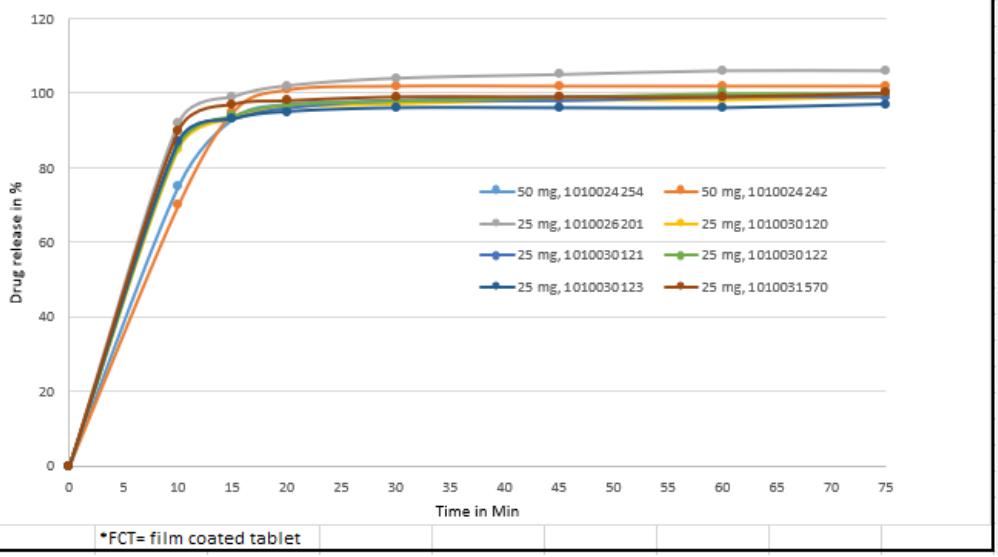
tablet (FCT) strengths 10 mg, 25 mg, 50 mg, and 100 mg were used to support clinical studies in different indications (see appendix 1 for details). For the indication in scope, the 25 mg dosage strength was used in phase 3 clinical studies. The final formulation manufactured at the selected commercial site was used throughout the phase 3 clinical studies and in registration stability study. Only (b) (4) components in the film coating are different which led to the color difference between the intended commercial formulation for 25 mg film coated tablet (FCT (light yellow)) and the final formulation used in clinical development (dark brown[5]. The Applicant used (b) (4) to obtain the film-coated tablets.

Additionally, a simplified debossing was introduced with the manufacture of the registration stability batches to ensure robust processing. These changes have been assessed, demonstrating that they do not affect the drug product in terms of the manufacture and critical quality attributes (CQAs). A comparative dissolution assessment of the two film-coated tablet formulations (clinical formulation 'dark brown' and commercial formulation 'light yellow') was conducted at three different pH levels (USP buffer pH 1.2, 4.5 and 6.8), demonstrating in vitro bioequivalence.

Applicant bridged the 50 mg FCT formulation (B# 1010024254, B# 1010024242 used in BA studies) and 25 mg FCT to be marketed formulation (B# 1010026201, 1010030120, 1010030121, 1010030122, 1010030123 and 1010031570 used in efficacy studies) via dissolution. Drug release is very rapid and dissolution profiles are similar. Overall, formulations have been bridged.

Figure 14: Bridging of formulations[6]:

	In QC method							
Time in Min	50 mg, 1010024254	50 mg, 1010024242	25 mg, 1010026201	25 mg, 1010030120	25 mg, 1010030121	25 mg, 1010030122	25 mg, 1010030123	25 mg, 1010031570
0	0	0	0	0	0	0	0	0
10	75	70	92	85	87	86	87	90
15	93	95	99	93	93	94	93	97
20	97	101	102	96	96	97	95	98
30	98	102	104	97	98	98	96	99
45	99	102	105	98	98	99	96	99
60	99	102	106	98	99	100	96	99
75	100	102	106	99	99	100	97	100



*FCT= film coated tablet

Recommendation:
From the Biopharmaceutics perspective, NDA-218436-ORIG-1 for Remibrutinib film-coated tablet, 25 mg is adequate.

List Submissions Being Assessed:

Document(s) Assessed	Date Received
Sequence 0000, Original submission	01/31/2025

Highlight of Key Issues from Last Cycle and Their Resolution: None.
Concise Description of Outstanding Issues*:* None.

Primary Biopharmaceutics Assessor's Name and Date:
Swapna Pamu, MS; 05/19/2025

Secondary Assessor Name and Date:
Tapash Ghosh, Ph.D. 06/06/2025

[5] \\CDSESUB1\EVSPROD\nda218436\0000\m3\32-body-data\32p-drug-prod\lou064-fct\32p2-pharm-dev\pharmaceutical-development-formulationdevelopment.pdf , pg 3
[6] \\CDSESUB1\EVSPROD\nda218436\0000\m3\32-body-data\32p-drug-prod\lou064-fct\32p2-pharm-dev\pharmaceutical-development-formulationdevelopment.pdf , pg 13, pg 51

APPENDIX 1

Formulation composition of 10 mg, 25 mg, 50 mg and 100 mg strengths[7]:

Dosage Strength		Amount per film coated tablet (mg)			
Ingredients	**Function**	**10 mg**	**25 mg**	**50 mg**	**100 mg**
(b) (4)					
Remibrutinib (free base)	Drug substance	10.000	25.000	50.000	100.000
Mannitol					
Copovidone					
(b) (4)					
Sodium lauryl sulfate					
(b) (4)					
Microcrystalline cellulose					
(b) (4)					
Croscarmellose sodium					
Sodium stearyl fumarate					
Tablet core weight					
Film-coated tablet weight		**95.000**	**136.051**	**272.100**	**544.200**

1 (b) (4)

[7] \\CDSESUB1\EVSPROD\nda218436\0000\m3\32-body-data\32p-drug-prod\lou064-fct\32p2-pharm-dev\pharmaceutical-development-formulationdevelopment.pdf , pg 5

Composition of remibrutinib, 25 mg film-coated tablets, clinical formulation vs. commercial formulation:

Ingredients	Function	Clinical formulation	Commercial formulation
		Amount per film coated tablet (mg)	
(b) (4)			
Remibrutinib (free base)	Drug substance	25.000	25.000
Mannitol	(b) (4)		(b) (4)
Copovidone			
(b) (4) Sodium lauryl sulfate			
(b) (4)			
Microcrystalline cellulose			
(b) (4)			
Croscarmellose sodium			
Sodium stearyl fumarate			
Tablet core weight			
(b) (4)			
Film-coated tablet weight		**136.051**	**136.050**
Debossing		**NVR / 84**	**LV / Novartis symbol**
Color		**dark brown**	**light yellow**

1 (b) (4)

APPENDIX 2

Individual unit dissolution data can be found here: \\CDSESUB1\EVSPROD\nda218436\0000\m3\32-body-data\32p-drug-prod\lou064-fct\32p2-pharm-dev\pharmaceutical-development-formulationdevelopment-mdr.pdf, page 51.

Swapna Pamu

Digitally signed by Swapna Pamu
Date: 6/06/2025 03:14:09PM
GUID: 5ab948e8002c8e63080fe7187098154c

Tapash Ghosh

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CRAIG M BERTHA
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