

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

217673Orig1s000

PRODUCT QUALITY REVIEW(S)

MEMORANDUM: DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC
HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH



DATE: 15-July-2025

TO: NDA 217673 Brensocatib Tablets File

FROM: Austin Yu, CMC Reviewer
OPQ/OPQA II/DPQA VII

SUBJECT: Shelf-life and stability assessment addendum memorandum regarding submission of longer stability data on (b) (4) formation.

BACKGROUND/EVALUATION:

(b) (4) was identified as an (b) (4) and controlled to (b) (4) ng/day (not more than (b) (4) ppm and (b) (4) ppm for the 25 mg and 10 mg strength tablets, respectively) in the drug product. Three 25 mg strength registration batches (CNDTZ, CNDVF, CNDVK) were observed to contain levels of (b) (4) exceeding the (b) (4) ppm at the (b) (4)-month time point. No earlier measurements of (b) (4) exist (b) (4)

Process Performance Qualification (PPQ) batches (CSVFN, CSVFP, CTGWV, 25 mg strength) were (b) (4) ppm and (CSVFK, CTGWS, CTGWT, 10 mg strength) (b) (4) (b) (4) ppm after (b) (4) months in long-term storage (25°C/60% RH). The Applicant suggested the cause of (b) (4) formation was due to (b) (4) (b) (4)

(b) (4) A 15-month shelf-life was granted in the interim because the Applicant previously submitted up to 3 months of accelerated stability data for 25 mg strength (b) (4) (b) (4) batches where the concentration of (b) (4) were (b) (4) ppm. In SDN 34/eCTD 0034 (submitted 2025 June 25), the Applicant provided up to 6 months and 2 months of both long-term and accelerated (b) (4) stability data for the 25 mg and 10 mg strength drug product, respectively, and included the following summary figure:

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In this submission, the Applicant requests a 24-month shelf life for both strengths of the drug product. For four 25 mg strength (b) (4) batches with up to 6 months of accelerated data (CVKYH, CVMCD, CVNBD, CVKYM), the (b) (4) concentration were (b) (4) ppm. Although it seems the formation of (b) (4)

this observation is not well justified when considering the sensitivity and quantitation limit (b) (4) ppm) of the Applicant's analytical method. For these four 25 mg strength (b) (4) batches, (b) (4)

(b) (4) The updated (b) (4) stability data well supports a 24-month shelf life for the 25 mg strength drug product.

For the 10 mg strength drug product, the lack of data from the (b) (4) batches is not ideal but we acknowledge that the average (b) (4) concentrations in the accelerated condition batches after 1 and 2 months are (b) (4) ($\pm$ (b) (4) ppm) and (b) (4) ($\pm$ (b) (4) ppm), respectively, (b) (4) the acceptance criterion for this DP strength (NMT (b) (4) ppm). In the 10 mg strength accelerated PPQ batches, the concentration of (b) (4) ranged from (b) (4) ppm at the 6-month time point in accelerated conditions. Considering the Applicant (b) (4) the (b) (4), we would expect the accelerated 10 mg strength batches to (b) (4) after 6 months in accelerated conditions and after 24 months in long-term conditions, much lower than the specification of no more than (b) (4) ppm. The monitoring for (b) (4) formation in the (b) (4) 10 mg strength batches is ongoing, but the recent data supports a 24-month shelf life.

¹ Carstensen JT. Stability of solids and solid dosage forms. *J Pharm Sci.* 1974;63(1):1-14. doi:10.1002/jps.2600630103

IQA Addendum Memorandum for NDA 217673

With the Applicant's updated measurements of (b) (4) formation in the accelerated conditions (b) (4) batches of the 25 mg strength DP, the rate of (b) (4) formation does not seem likely to exceed the acceptance criterion of NMT (b) (4) ppm by 24 months for long-term storage batches. Furthermore, based on the accelerated PPQ 10 mg strength DP batches and updated measurements of (b) (4) formation in the accelerated conditions (b) (4) batches of the 10 mg strength DP, the formation of (b) (4) does not seem likely to exceed the acceptance criterion of NMT (b) (4) ppm by 24 months for long-term storage batches. The (b) (4) to brensocatib ratio for the 10 mg strength tablets is greater than that of the 25 mg strength tablets (b) (4) implying a greater potential to form the (b) (4) in the 10 mg strength tablets. (b) (4)

(b) (4) In the accelerated conditions stability data for the original registration batches of both strengths of DP, the concentrations of (b) (4) degradant, total impurities, and (b) (4) remain below the specification limit at the end of the 6-months of monitoring. Measurements of the (b) (4) degradant, total impurities, and (b) (4) also remain below the specification limit in all the registration batches in long-term conditions in up to 24 months and up to 18 months for the 25 mg and 10 mg strength DP batches, respectively. Considering the available stability data, and the fact that the Applicant has committed to monitor and discuss with the Agency any out-of-specification results, **it is reasonable to grant the 24-month shelf-life proposed in the interim.**

In SDN 34/eCTD 0034, the Applicant submitted minor changes in P.3 Manufacture and P.4 Control of Excipients. The Applicant specifies in P.3 that the film-coated tablets (b) (4). In P.4, the Applicant re-iterates that all excipients used in the manufacture of the DP are of USP/NF quality. In addition, the Applicant includes an additional control for the (b) (4) excipient of (b) (4) content NMT (b) (4) ppm as per the supplier's CoA. The Applicant included an example of the supplier's CoA in P.4.4 which documents a measurement of the (b) (4) content in the (b) (4). In SDN 36/eCTD 0036 (submitted 2025 July 11), the Applicant corrected the total impurities measurement typo at the 1-month timepoint in Table 73 of the P.8.3 stability data. Previously, this measurement lacked the decimal and therefore far exceeded the acceptance criterion. These changes are adequate for CMC.

RECOMMENDATION TO DPACC FROM CMC: Approve

Austin Yu
CMC Reviewer

cc:
Orig. NDA 217673
OPQ/OPQAI/DPQAVIII/CBertha

IQA Addendum Memorandum for NDA 217673

OPQ/OPQAII/DPQAVII/AYu
OTS/OB/DBIII/EShives
OND/OII/DPACC/EFerre
OTS/OCF/DIIP/LHe
OMP/OPDP/DPP/PRG3/QCapasso
OND/OII/DPT-II/JRoy
OSE/OSEIO/OSEIO PMS/CAttinello
OMP/OPDP/DPP/PRG3/AAdeleye
OND/ORO/DRO-II/TYung
OPQ/OPRO/DRBPMII/EGimose
OPQ/OPQAIII/DPQAXVIII/LPerez
OPQ/OPQAIII/DPQAXVIII/SBain
OPQ/OPMA/DPMAIII/JDu
OPQ/OPMA/DPMAIII/SYang
OPQ/OPQAII/DPQAXII/TGhosh
OPQ/OPQAII/DPQAXII/KNahar

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/s/

AUSTIN S YU
07/15/2025 11:35:32 AM

CRAIG M BERTHA
07/15/2025 12:02:17 PM
I concur.

MEMORANDUM: DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC
HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 05-June-2025
TO: NDA 217673 Brensocatib Tablets File
FROM: Austin Yu, CMC Reviewer
OPQ/OPQA II/DPQA VII



SUBJECT: Stability assessment addendum memorandum
regarding submission of longer stability data on (b) (4)
(b) (4) formation.

BACKGROUND/EVALUATION:

(b) (4) was identified as an (b) (4) and controlled to (b) (4) ng/day (not more than (b) (4) ppm and (b) (4) ppm for the 25 mg and 10 mg strength tablets, respectively) in the drug product. Three 25 mg strength registration batches (CNDTZ, CNDVF, CNDVK) were observed to contain levels of (b) (4) exceeding the (b) (4) ppm at the 1 month time point. No earlier measurements of (b) (4) exist (b) (4).

Process Performance Qualification (PPQ) batches (CSVFN, CSVFP, CTGWV, 25 mg strength) were (b) (4) ppm and (CSVFK, CTGWS, CTGWT, 10 mg strength) (b) (4) ppm after (b) (4) months in long-term storage (25°C/60% RH). The Applicant suggested the cause of (b) (4) formation was due to (b) (4) (b) (4).

A 15-month shelf-life was granted in the interim because the Applicant previously submitted up to 3 months of accelerated stability data for 25 mg strength (b) (4) batches where the concentration of (b) (4) were (b) (4) ppm. The Applicant provided up to 5 months and 1 month of accelerated (b) (4) stability data for the 25 mg and 10 mg strength drug product, respectively, and included the following summary figure:

IQA Addendum Memorandum for NDA 217673

For four 25 mg strength (b) (4) batches with up to 5 months of accelerated data (CVKYH, CVMCD, CVNBG, CVKYM), the average (b) (4) concentration at the 3, 4, and 5-month time points were (b) (4) $\pm$ (b) (4) ppm, (b) (4) $\pm$ (b) (4) ppm, and (b) (4) $\pm$ (b) (4) ppm, respectively. The additional months of accelerated (and long-term) (b) (4) (b) (4) stability data for the 25 mg strength (b) (4) batches provide additional support for the requested 15-month shelf life. The concentration of (b) (4) (b) (4) in accelerated batches appears to (b) (4)

(b) (4) which is (b) (4) below the acceptance criterion of NMT (b) (4) ppm. The updated stability data well supports a 15-month shelf life for the 25 mg strength drug product.

For the 10 mg strength drug product, the lack of data from the (b) (4) batches is not ideal but we acknowledge that the average (b) (4) concentrations in the accelerated condition batches after one month is (b) (4) $\pm$ (b) (4) ppm, (b) (4) the acceptance criterion for this DP strength (NMT (b) (4) ppm). In the 10 mg strength accelerated PPQ batches, the concentration of (b) (4) ranged from (b) (4) (b) (4) ppm at the 6-month time point in accelerated conditions. Considering the Applicant (b) (4) we would expect the accelerated 10 mg strength batches to (b) (4) after 6 months in accelerated conditions and after 15 months in long-term conditions, much lower than the specification of no more than (b) (4) ppm. The monitoring for (b) (4) formation in the (b) (4) 10 mg strength batches is ongoing, but the recent data supports a 15-month shelf life.

With the Applicant's updated measurements of (b) (4) formation in the accelerated conditions (b) (4) batches of the 25 mg strength DP, the rate of (b) (4) formation does not seem likely to exceed the acceptance criterion of NMT (b) (4) ppm by 15 months for long-term storage batches. Furthermore, based on the accelerated PPQ 10 mg strength DP batches and updated measurements of (b) (4) formation in the accelerated conditions (b) (4) batches of the 10 mg strength DP, the formation of (b) (4) (b) (4) does not seem likely to exceed the acceptance criterion of NMT (b) (4) ppm by 15 months for long-term storage batches. The (b) (4) to brensocatib ratio for the 10 mg strength tablets is (b) (4) than that of the 25 mg strength tablets (b) (4) (b) (4) (b) (4) This

¹ Carstensen JT. Stability of solids and solid dosage forms. *J Pharm Sci*. 1974;63(1):1-14. doi:10.1002/jps.2600630103

(b) (4) Considering the available data, and the fact that the Applicant has committed to monitor and discuss with the Agency any out-of-specification results, **it is reasonable to continue to grant the 15-month shelf-life proposed in the interim.**

RECOMMENDATION TO DPACC FROM CMC: Approve

Austin Yu
CMC Reviewer

cc:
Orig. NDA 217673
OPQ/OPQAII/DPQAVIII/CBertha
OPQ/OPQAII/DPQAVII/AYu
OTS/OB/DBIII/EShives
OND/OII/DPACC/EFerre
OTS/OCP/DIIP/LHe
OMP/OPDP/DPP/PRG3/QCapasso
OND/OII/DPT-II/JRoy
OSE/OSEIO/OSEIO PMS/CAttinello
OMP/OPDP/DPP/PRG3/AAdeleye
OND/ORO/DRO-II/TYung
OPQ/OPRO/DRBPMII/EGimose
OPQ/OPQAIII/DPQAXVIII/LPerez
OPQ/OPQAIII/DPQAXVIII/SBain
OPQ/OPMA/DPMAIII/JDu
OPQ/OPMA/DPMAIII/SYang
OPQ/OPQAII/DPQAXII/TGhosh
OPQ/OPQAII/DPQAXII/KNahar

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/s/

AUSTIN S YU
06/05/2025 10:21:27 AM

CRAIG M BERTHA
06/06/2025 06:29:02 AM



Title:	New Drug Application (NDA) Integrated Quality Assessment Template		
Document ID:	OPQ-ALL-TEM-0004		
Effective Date:	04 Nov 2022	Revision:	08
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Office of Pharmaceutical Quality

New Drug Application (NDA) 217673 Integrated Quality Assessment



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RECOMMENDATION

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

NDA 217673 Assessment #1

Drug Product Name	Brensocatib Tablets
Dosage Form	Tablets
Strength	25 mg/tablet
Route of Administration	oral
Rx/OTC Dispensed	Rx
Applicant	Insmed Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original (SD-1)	12-Dec-2024	All
Amendment (SD-16)	06-Mar-2025	Manufacturing/facilities
Amendment (SD-17)	07-Mar-2025	Biopharmaceutics and Manufacturing/facilities
Amendment (SD-22)	28-Mar-2025	All
Amendment (SD-23)	03-Apr-2025	Drug product
Amendment (SD-24)	04-Apr-2025	Labeling
Amendment (SD-26)	11-Apr-2025	Manufacturing/facilities
Amendment (SD-30)	28-Apr-2025	Drug product

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Sam Bain	Lawrence Perez
Drug Product	Austin Yu	Craig M. Bertha
Manufacturing	Du Ju	Shu-Wei Yang
Microbiology	N/A	
Biopharmaceutics	Kamrun Nahar	Tapash Ghosh
Labeling	Austin Yu	Julia Pinto



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U.S. FOOD & DRUG
ADMINISTRATION

Template Revision: 03

Regulatory Business Process Manager	Emma Gimose	
Application Technical Lead	Craig M. Bertha	
Laboratory (OTR)	N/A	
Environmental	Austin Yu	Craig M. Bertha

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[Manufacturing/Facilities](#)

[Biopharmaceutics](#)

[Labeling](#)



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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)	III	(b) (4)	(b) (4)	N/A	N/A	Sufficient information in application
	III			N/A	N/A	Sufficient information in application
	III			N/A	N/A	Sufficient information in application

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

Document	Application Number	Description
IND	(b) (4)	(b) (4) IND for information regarding bresocaticb

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH	N/A			
Clinical	N/A			
Other				



Title:	NDA IQA Template Title Page- EXEC SUMMARY		
Document ID:	OPQ-ALL-TEM-0040		
Effective Date:	26 Sep 2023	Revision:	00
Total Pages:	7		



Template Revision: 03

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Office of Pharmaceutical Quality

New Drug Application (NDA) 217673 Integrated Quality Assessment

NDA Executive Summary

1. Application/Product Information

NDA Number	217673		
Applicant Name	Insmed, Inc.		
Drug Product Name	Brensocatib Tablets		
Dosage Form	Tablet		
Proposed Strength(s)	25 mg/tablet		
NDA Classification	Type 1 - NME		
Route of Administration	Oral		
Maximum Daily Dose	25 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	Treatment of non-cystic fibrosis bronchiectasis (NCFBE) in adult and pediatric patients 12 years of age and older		
Drug Product Description	The drug product is a gray, round, film-coated tablet which is debossed with "25" on one side and "BRE" on the other		
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°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store in original container.		
Review Team	Discipline	Primary	Secondary
	<i>Drug Substance</i>	Sam Bain	Lawrence Perez
	<i>Drug Product</i>	Austin Yu	Craig M. Bertha
	<i>Manufacturing</i>	Du Ju	Shu-Wei Yang

	<i>Biopharmaceutics</i>	Kamrun Nahar	Tapash Ghosh
	<i>Microbiology</i>	N/A	
	<i>Other (specify)</i>	N/A	
	<i>Labeling</i>	Austin Yu	Julia Pinto
	<i>RBPM</i>	Emma Gimose	
	<i>ATL</i>	Craig M. Bertha	
Consults	N/A		

2. Final Overall Recommendation - **Approval**

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? Yes

Recommendation by Subdiscipline:

Drug Substance - **Adequate**
Drug Product - **Adequate**
Quality Labeling - **Pending¹**
Manufacturing - **Adequate**
Biopharmaceutics - **Adequate**
Microbiology - **N/A**

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

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No

Comments:

¹The 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.

**Comparability Protocols (PACMP): No
Comments:**

Additional Lifecycle Comments: N/A

CMC Review Summary

Drug Substance

The drug substance, brensocatib, is manufactured in a (b) (4) synthesis that (b) (4). There are three defined regulatory starting materials that are consistent with the recommendations of ICH Q11. Synthetic schemes as well as the specifications, test procedures, and analyses data for the starting materials are provided and they are adequate. In addition, sufficient information for the drug substance synthesis is also provided, which include the synthetic scheme, narrative descriptions, critical process parameters, in-process controls, and specifications for the (b) (4), as well as information about the development of the synthesis.

The drug substance is structure is characterized with typical spectrometric techniques. In addition, single-crystal x-ray diffraction results also support the structure and absolute configuration of the two chiral centers of the drug substance.

The NDA includes adequate information for potential and observed impurities in the drug substance. As the drug substance contains (b) (4) (b) (4) (b) (4) the applicant has confirmed that the levels of (b) (4) in the drug substance are well below the Acceptable Intake (AI) amount confirmed by the non-clinical team. In addition, the applicant has demonstrated that mutagenic and other (b) (4) impurities are purged during the synthesis to levels that are considered to be safe. The elemental impurity (b) (4) is included in the drug substance specification with a limit that is within the recommendations of ICH Q3D. The drug substance specification is also consistent with the recommendations outlined in ICH Q6A, Q3C and Q3D. The acceptance criteria limits that are above the ICH Q3A qualification threshold for various specified ordinary organic impurities, have been found to be acceptable by the non-clinical team.

Sufficient information has been provided in support of the reference standards necessary for analysis of the drug substance.

The drug substance container closure system is typical of those accepted by the Agency for solid drug substances. Stability data provided for the drug substance supports a (b) (4) month retest period for storage between (b) (4) °C.

The NDA is recommended for approval from the drug substance CMC perspective.

(b) (4) impurity, the applicant submitted up to 3 months of long-term and accelerated stability data for multiple supportive batches of the 25 mg strength product manufactured with (b) (4). Based on the totality of the data and the fact that the applicant has committed to monitor and discuss any OOS results with the Agency, it is reasonable to **grant the 15 month shelf-life proposed in the interim**, as more data are being collected.

Manufacturing/Facilities

The manufacturing process for both strengths of BRINSUPRI (brensocatib) tablet drug product includes (b) (4).

(b) (4) The registration batches and the proposed commercial batches have the same manufacturing process.

Batch size comparison between the registration batch and commercial batch:

The registration batches for both strengths, e.g., bulk batch CMXTP (25 mg strength in seq#0001) and batch CMNYC (10 mg strength, added in seq#0017), are same, i.e., (b) (4) tablets per batch or about (b) (4) kg per batch, and the proposed commercial batch size is (b) (4) per batch or about (b) (4) kg per batch. The scale up is (b) (4) fold from registration stability to commercial batches.

Scale up commercial size batches:

To support the scale up, the applicant manufactured scale-up commercial size batches (b) (4) kg) by (b) (4).

The associated data for these 5 commercial size batches are presented in “Manufacturing Process Development” report in 3.2.P.2 and have been evaluated. In summary, the proposed equipment, process parameters and in-process control/test specification ranges are justified by these 5 commercial size batches.

The drug substance and drug product manufacturing facilities are found acceptable based on inspection history.

Biopharmaceutics

The biopharmaceutics review focused on the evaluation of the adequacy of the overall information/data supporting the dissolution method and acceptance criteria as well as the bridging of formulation changes made during development.

The dissolution method uses USP Apparatus 2 (paddle) with rotation speed of 65 rpm, 500 mL of 0.1 N hydrochloric acid medium at 37°C and an acceptance criterion of Q = (b) (4) % in 30 minutes. The method is found to be adequate for drug release testing of the drug product as per specification.

BRINSUPRI (brensocatib) tablets are immediate release film-coated tablets with two strengths (10 and 25 mg) and these were used in the Phase 2 and Phase 3 studies as well as a majority of Phase 1 studies. Phase 2 tablets and Phase 3 tablets (10 mg, and 25 mg) have the (b) (4)

The intended respective commercial formulations of 10 and 25 mg strength tablets are (b) (4) used across the clinical development program, however (b) (4) used in the clinical studies to gray debossed tablets for the commercial drug product. The drug substance used in the Phase 2 tablets was manufactured at (b) (4). For the Phase 3 tablets and intended commercial tablet formulations, the drug substance manufacturing site was transferred to Esteve Quimica, SA, Spain (Esteve). During clinical phase 2, the drug product manufacturing site also changed from (b) (4), to Patheon, Ontario, Canada. To bridge the tablets used during development and the commercial drug product, comparative dissolution studies were conducted to compare the dissolution profiles of Phase 2, Phase 3, and commercial drug product at pHs of 1, 2, 4.5, and 6.8 using the quality control dissolution method conditions. Based on the results, the applicant adequately bridged the clinical and commercial formulation drug products.

From a biopharmaceutics perspective the application is recommended for approval.

Application Technical Lead Name and Date:

Craig M. Bertha, CMC Reviewer/ATL, 09-May-2025

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BIOPHARMACEUTICS**NDA:** NDA 217673-Orig-1**Drug Product Name / Strength:** Brinsupri® (Brensocatib) tablets, 10 mg, 25 mg.**Route of Administration:** Oral**Applicant Name:** Insmel Incorporated**Indication:** BRINSUPRI is indicated for the treatment of non-cystic fibrosis bronchiectasis in adult and pediatric patients 12 years of age and older**Submission date:** 12/12/2024**Primary Reviewer:** Kamrun Nahar, Ph.D.**Secondary Reviewer:** Tapash Ghosh, Ph.D.**Recommendation:** Adequate**BACKGROUND:**

The Applicant is seeking approval under 505(b)(1) regulatory pathways for the NDA 217673, Brinsupri® (Brensocatib) immediate release tablets, 10 mg, 25 mg, for oral administration. Biopharmaceutics review was focused on the evaluation of the adequacy of the overall information/data supporting: 1) the proposed dissolution method and acceptance criteria, and 2) formulation bridging throughout product development. Summary of the key findings are presented below, based on the review of the provided information/data:

1) Dissolution Method and Acceptance Criteria: Adequate

Approved dissolution method and acceptance criterion for quality control testing of the proposed Brinsupri® (Brensocatib) tablets, 10 mg, 25 mg at release and stability:

Apparatus	Rotation Speed (rpm)	Medium	Volume (mL)/ Temperature	Dissolution acceptance criteria
USP Apparatus 2 (Paddle)	65	0.1NHCl	500/ 37.0°±0.5°C	Q= (b) (4) % in 30 minutes

2) Bridging of Formulations: Adequate

Brinsupri® (Brensocatib), 10 mg and 25 mg are an immediate release film-coated tablet formulations which were used in the Phase 2 and Phase 3 studies as well as a majority of Phase 1 studies. The intended commercial formulation of 25 mg is (b) (4) (b) (4) used across the clinical development program, except for (b) (4) were used in the clinical studies which were changed to grey debossed tablets on both sides for the commercial drug product. The drug substance used in the Phase 2 tablets was manufactured at (b) (4) For the Phase 3 tablets and intended commercial tablet formulations, the drug substance manufacturing site was transferred to Esteve Quimica, SA, Spain (Esteve). Phase 2 tablet formulation and Phase 3 tablets, 10 mg, and 25 mg, (b) (4) (b) (4) Comparative dissolution studies were conducted to compare the dissolution profiles of Phase 2 with Phase 3 and commercial drug

product at pHs of 1, 2, 4.5, and 6.8 using QC dissolution method conditions. The Applicant adequately bridged the clinical and commercial formulations.

3) Alcohol dose dumping: Not applicable

Since the proposed product is an immediate release tablet, alcohol dose dumping study is not required.

4) Biowaiver request: Not applicable

The Applicant used both strengths of for Brinsupri® (Brensocatib) tablets, 10 mg, 25 mg in phase 3 studies and did not request for biowaiver.

CONCLUSION AND RECOMMENDATION:

Form a Biopharmaceutics perspective, NDA 217673 for Brinsupri® (Brensocatib) tablets, 10 mg, 25 mg is **adequate** for approval.

BIOPHARMACEUTICS ASSESSMENT:

List Submissions being reviewed:

Sequence 0001: 12/12/2024

Sequence 0016: 03/06/2025

Description and composition of the drug product:

Brinsupri® (Brensocatib) tablets, 10 mg, 25 mg are an immediate release film-coated tablet for oral administration.

Solubility:

The Applicant claimed that Brensocatib is classified as a BCS class I compound, i.e., highly soluble, and highly permeable compound. Solubility data of Brensocatib showed high solubility across the physiological pH conditions, i.e., pH 1.2-6.8.

Table 1: Solubility of Brensocatib, 25 mg in 250 mL at 37.0±1.0°C in different pH

Media	Time Point (hrs)	Final pH	Sample Solubility (mg/mL)	Mean Solubility (mg/mL)/RSD (%)	Mean D/S (mL)
pH 1.2 HCl/KCl	24	1.17	0.264, 0.263, 0.267	> 0.265/0.76	< 94.34
	48	1.21	0.263, 0.258, 0.262	> 0.261/0.94	< 95.79
pH 2.0 HCl/KCl	24	2.01	0.272, 0.270, 0.279	> 0.274/1.90	< 91.24
	48	2.01	0.268, 0.279, 0.271	> 0.273/2.09	< 91.58
pH 4.5 Acetate Buffer	24	4.53	0.263, 0.265, 0.266	> 0.265/0.43	< 94.34
	48	4.50	0.265, 0.267, 0.265	> 0.266/0.43	< 93.98
pH 6.0 Phosphate Buffer	24	5.99	0.248, 0.258, 0.254	0.253/2.01	98.81
	48	5.99	0.250, 0.253, 0.258	0.254/1.57	98.43
pH 6.8 Phosphate Buffer	24	6.77	0.166, 0.163, 0.166	0.165/1.11	151.52
	48	6.79	0.172, 0.167, 0.169	0.170/1.43	147.06
pH 8.1 Alkaline Borate	24	8.09	0.030, 0.028, 0.028	0.029/3.87	862.07
	48	8.12	0.033, 0.033, 0.031	0.033/3.23	757.58

D/S: dose (25 mg) / mean solubility (NMT 250 mL)

Drug substance (DS) particle size and distribution (PSD):

The manufacturing process of the Brensocatib monohydrate produces (b) (4) drug substance (b) (4). Brensocatib monohydrate is a highly soluble compound. Hence, the risk of DS PSD on dissolution is low.

Table 2: Particle Size Distribution of Brensocatib Drug Substance

Batch Number (Use)	D ₁₀ (µm)	D ₅₀ (µm)	D ₉₀ (µm)
19-401 (clinical)	(b) (4)		
19-402 (clinical)			
20-401 (clinical)			
20-402 (clinical)			
000001 (clinical)			
000002 (clinical)			
100001 (registration)			
100002 (registration)			
100003 (registration)			
100004 (Scale up development)			
100005 (PPQ)			
100006 (PPQ)			
100007 (PPQ)			

Development of dissolution method:

(b) (4)

Discrimination ability of the dissolution method:

The Applicant submitted information related to discriminating ability by changing drug substances (DS) particle size distribution (PSD) and (b) (4)

Drug substances (DS) particle size distribution (PSD):

the Applicant submitted discriminating ability information due to the differences in drug substances (DS) particle size distribution (PSD) and dissolution. Dissolution data of both strengths, i.e., 10 mg and 25 mg of the proposed product did not show any differences in drug release due to the change in DS PSD (i.e., DS PSD clinical batch# 20-402 with d_{10} (b) (4) d_{50} (b) (4) and d_{90} (b) (4) microns vs DS PSD, registration batch# 100003 with d_{10} (b) (4) d_{50} (b) (4) and d_{90} (b) (4) microns).

Figure 10: Dissolution Comparison of 25 mg Tablet

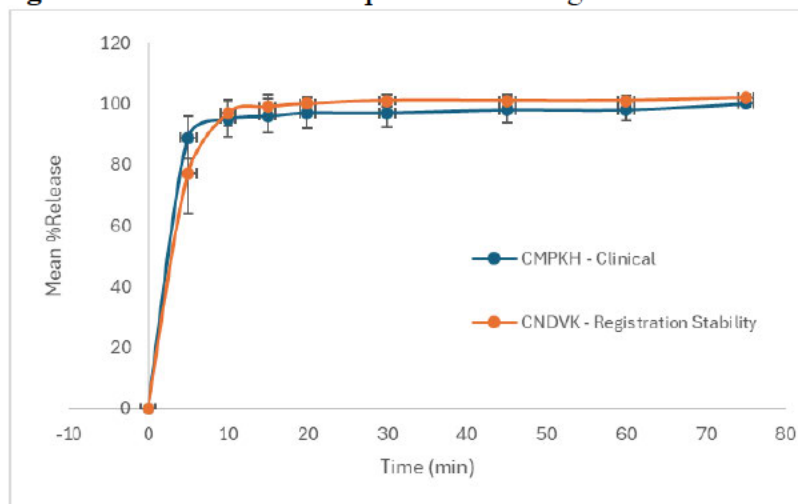
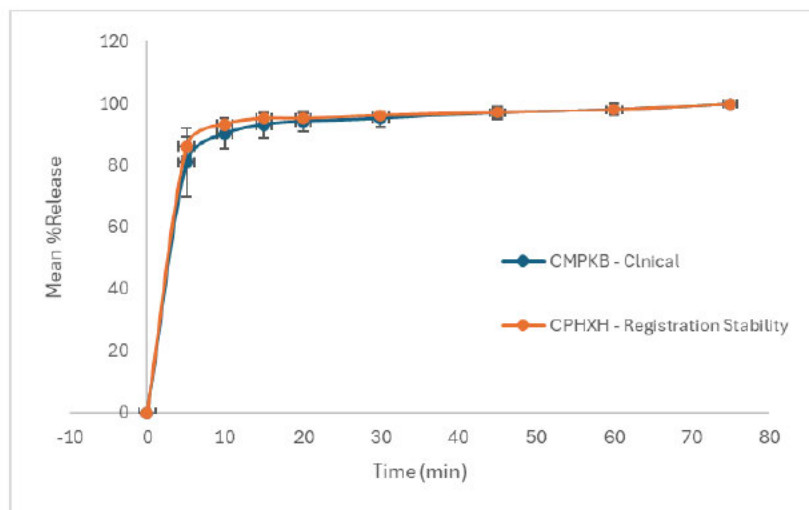
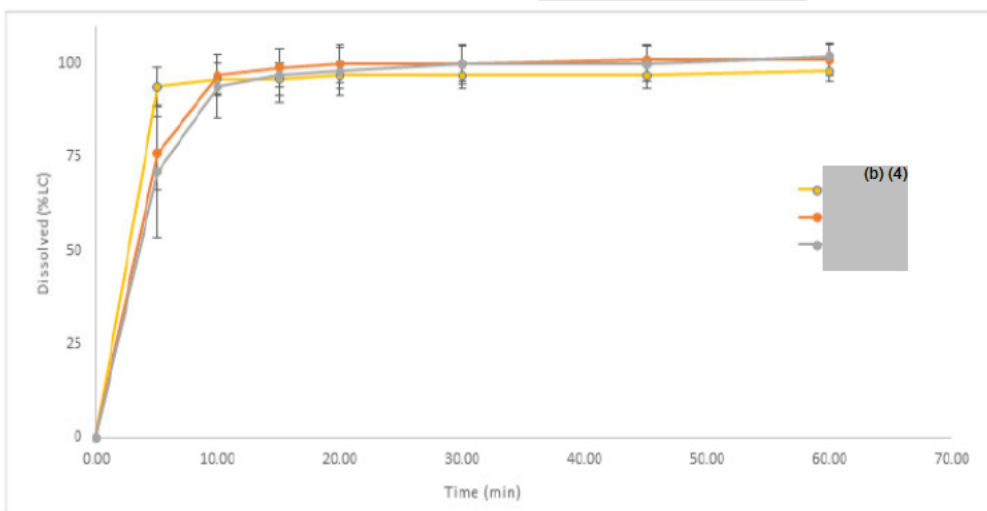


Figure 11: Dissolution Comparison of 10 mg Tablet

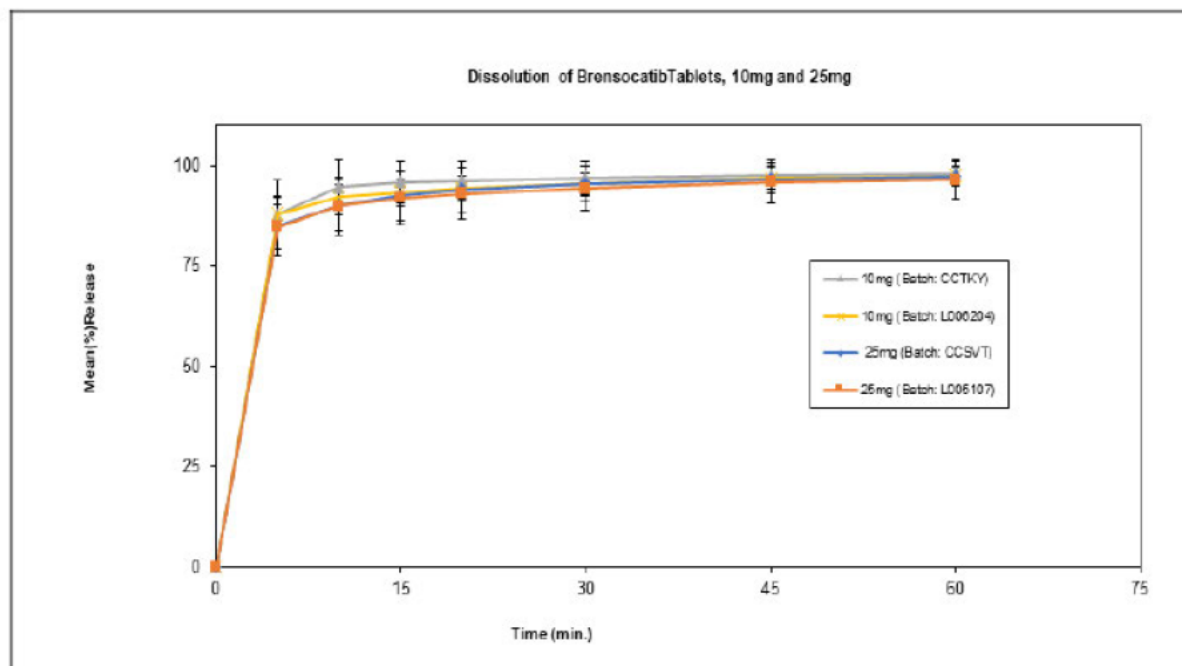
A dissolution study was conducted to assess the impact of the tablet (b) (4) on the dissolution profile of the drug product. For this study, the 25 mg tablets (batch CDGCB) were used. (b) (4) during manufacturing. The dissolution profiles (Apparatus II, 500 mL, 0.1N HCl, 65 rpm) at different (b) (4) did not show any significant change in drug release due to the difference in tablet (b) (4).

Table 12: Dissolution Profiles of Different (b) (4)**Suitability of the Dissolution Method for Different Tablet Strengths:**

The Applicant evaluated the suitability of the dissolution method for both strengths, i.e., 10 mg, and 25 mg. Dissolution profiles for different tablet strengths (10 mg and 25 mg) did not show

any significant changes in the dissolution profiles across the tablet strengths indicating suitability for both strengths of the tablets, 10 mg, and 25 mg.

Figure 12: Comparison of Dissolution Profiles for Different Tablet Strengths



Conclusion:

Overall, Brensocatib is a highly soluble. The Applicant provided dissolution method development and validation report. The Applicant optimized the dissolution method conditions; dissolution method did not show discriminating ability due to the change in drug substance particle size distribution and tablet (b) (4). However, given the high solubility and permeability of Brensocatib, risk is considered low. The parameters selected are based on the standard dissolution testing conditions in FDA guidance (Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances, August 2018) with the modification of the paddle speed (b) (4). Therefore, based on the totality of the information, dissolution method and acceptance criterion as described below is adequate.

Dissolution acceptance criterion:

The Applicant proposed the dissolution acceptance criteria as “Q = (b) (4)% in 30 minutes”. Dissolution data showed very rapid drug release, i.e., (b) (4)% is released in (b) (4) minutes. Therefore, based on the dissolution data, the Applicant’s proposed dissolution acceptance criterion is deemed adequate. Dissolution acceptance criterion is set as “Q = (b) (4)% in 30 minutes”.

Approved dissolution method and acceptance criteria for the proposed Brinsupri® (Brensocatib) tablets, 10 mg, 25 mg:

Apparatus	Rotation Speed (rpm)	Medium	Volume (mL)/ Temperature	Dissolution acceptance criterion
USP Apparatus 2 (Paddle)	65	0.1N HCl	500/ 37±0.5°C	Q = $\frac{(b)(4)}{(4)}$ % in 30 minutes

Formulation development and bridging:

An oral liquid formulation in the concentration range of (b) (4) mg/mL was initially developed for the early clinical studies, subsequently (b) (4) film-coated tablets were developed for use in Phase 1, Phase 2, and Phase 3 clinical studies in three strengths: 10 mg, 15 mg, and 25 mg, and 40 mg. Brensocatib tablets, 10 mg, and 25 mg are the proposed strengths.

Drug substance manufacturing site change:

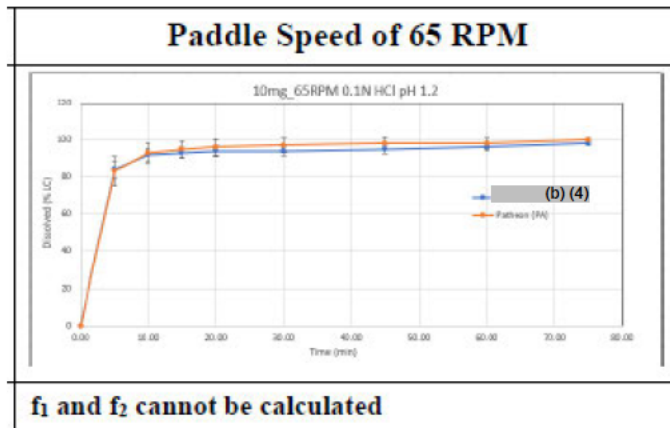
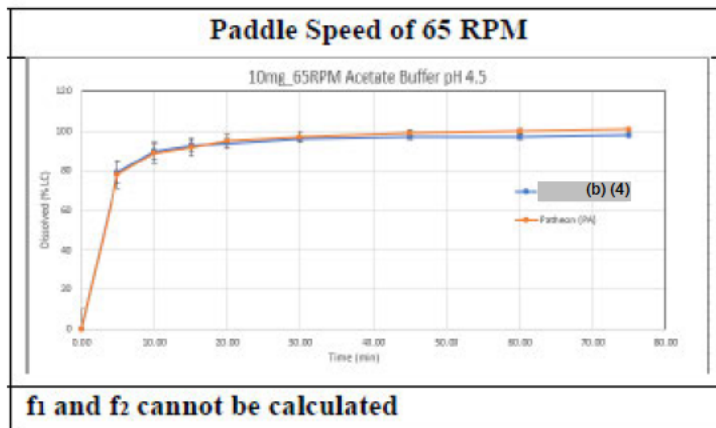
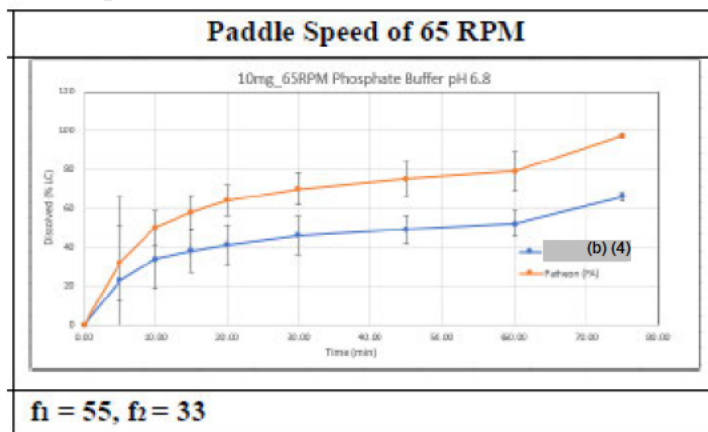
The drug substance used in the Phase 2 tablets was manufactured at (b) (4). For the Phase 3 tablets and intended commercial tablet formulations, the drug substance manufacturing site was transferred to Esteve Quimica, SA, Spain (Esteve). The manufacturing process used by (b) (4) is the same as the manufacturing process used by Esteve Quimica, except for (b) (4). (b) (4).

Tablet manufacturing site change and comparison Between Phase 2 Tablets and Phase 3 Tablets:

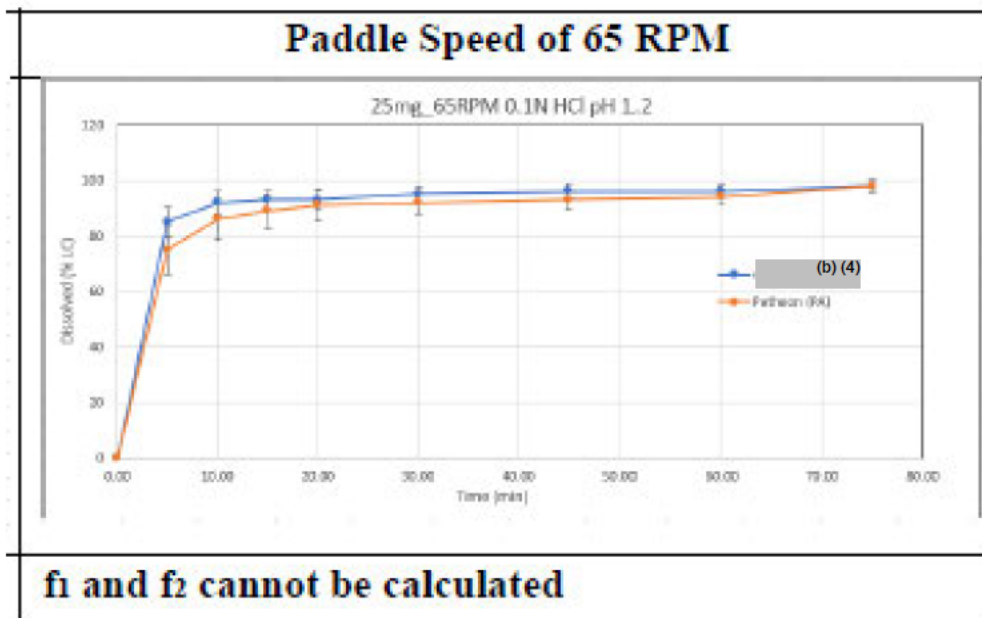
The compositions of the core tablets for the Phase 2 and Phase 3 tablets are (b) (4). (b) (4). (b) (4). The Applicant provided comparative dissolution data of the core and coated tablets of 10 mg, and 25 mg which showed similar drug release. The Applicant stated that (b) (4). (b) (4).

Initially, the Phase 2 tablets were manufactured at (b) (4) to support Phase 1 and Phase 2 clinical studies. The manufacturing site was changed to Patheon Inc., Whitby, ON, Canada to support Phase 3 clinical studies and the intended commercial product.

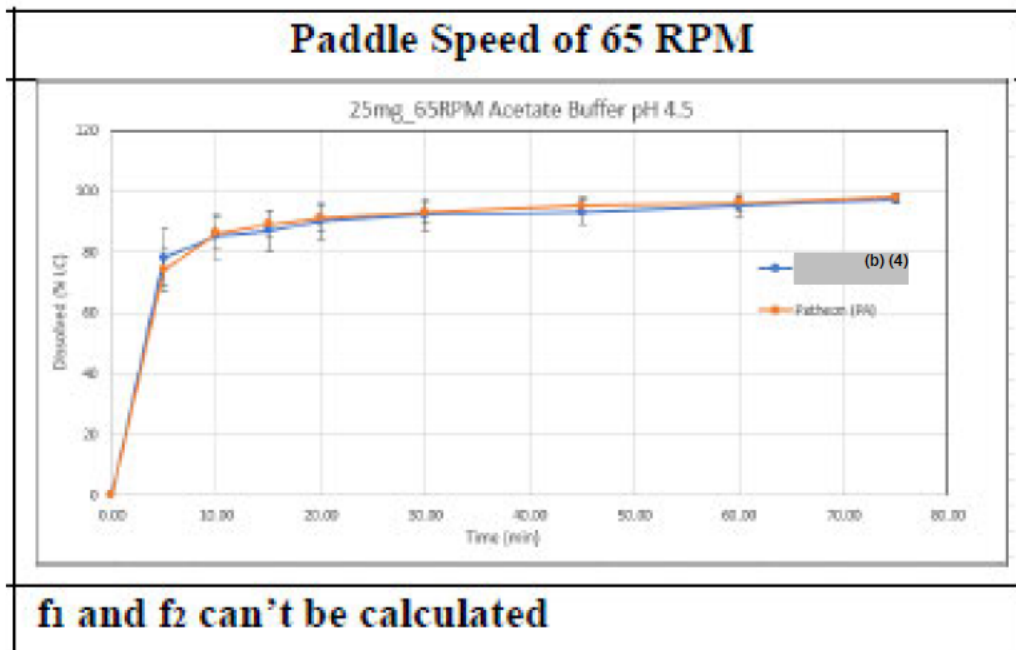
(b) (4). (b) (4). (b) (4). (b) (4). (b) (4). The Applicant provided comparative dissolution data of the tablets manufactured at (b) (4) vs Patheon, Canada.

Figure 13: Dissolution Comparison for 10 mg Tablets**a. pH 1.2****b. pH 4.5****c. pH 6.8****Figure 14: Dissolution Comparison for 25 mg Tablets**

a. pH 1.2



b. pH 4.5



c. pH 6.8

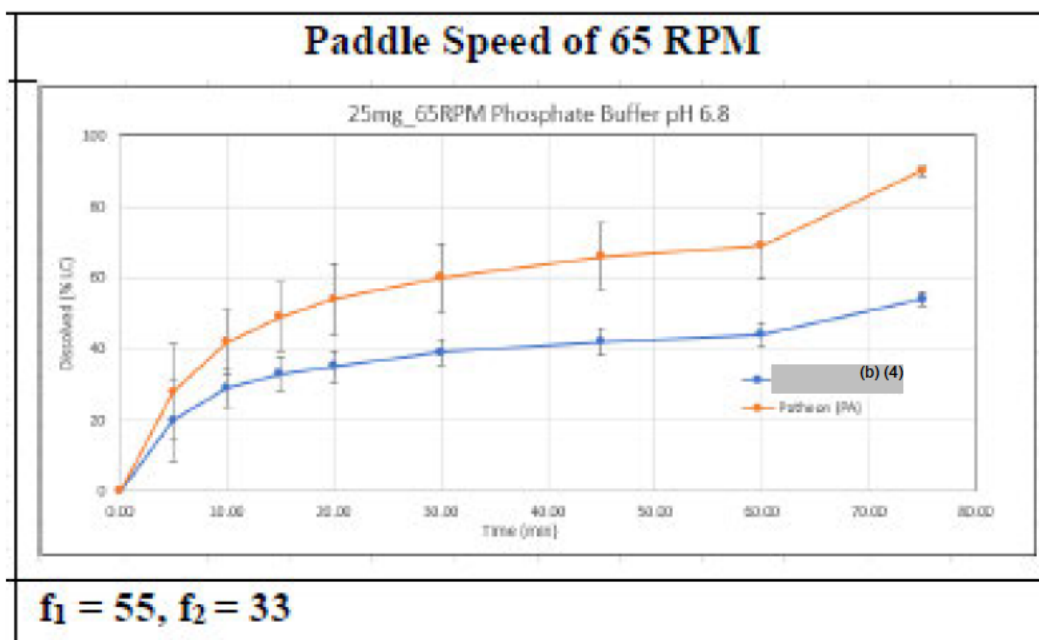
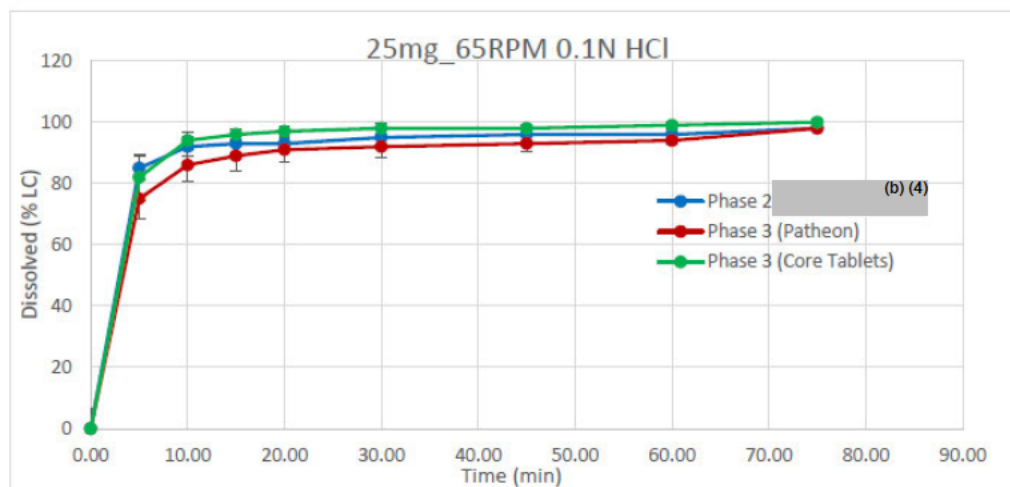


Figure 15: Dissolution Results for Phase 2, Phase 3, and Phase 3 Core Tablets (25 mg)



In summary, Brensocatib drug substance has high solubility in the pH range of 1.2-6.8, DS PSD has no significant impact on dissolution. The compositions of (b) (4) (b) (4) for both Phase 2 and Phase 3 tablets. The manufacturing process is (b) (4) (b) (4). The major difference is (b) (4) (b) (4) used in the Phase 2 and Phase 3 tablets. Drug products showed very rapid drug release at pH 1.2. The Applicant also provided additional comparative dissolution data in pH 4.5 and pH 6.8. Dissolution data at pH 4.5 is also very rapid between phase 2 and phase 3 formulations. At pH 6.8, dissolution data showed that formulation manufactured in (b) (4) has lower drug release compared to the formulation manufactured in Patheon. The Applicant justified the potential root cause for the differences in the dissolution profiles at pH 6.8 might be attributed to (b) (4) and the differences in dissolution rate of Phase

2 tablets and Phase 3 tablets at pH 6.8 is not clinically relevant as Brensocatib oral absorption is not affected by the solubility and dissolution rate. Since, the tablets from (b) (4) and Patheon showed very rapid release in pH 1.2 which meets the requirement for the SUPAC IR FDA guidance, slight difference in drug release in pH 6.8 is considered acceptable. The Applicant also submitted comparative dissolution data of the Phase 2 tablets, Phase 3 tablets and Phase 3 core tablet which showed very rapid drug release from the tablets in QC dissolution method.

Comparison Between Phase 3 and Commercial Tablets:

Phase 3 tablets and the intended commercial tablet formulations:

The compositions of the core tablets between the Phase 3 tablets and the intended commercial tablet formulations (b) (4) (b) (4)

(b) (4) The film coating color for the Phase 3 tablets is (b) (4) for both the 10 mg and the 25 mg tablets, while the colors selected for the commercial tablets are brown for the 10 mg tablet and gray for the 25 mg tablet. The commercial tablets are debossed with one side as "BRE" and the other side as "10" or "25" depending on the tablet strength. The manufacturing site and process are the same for both tablet formulations. (b) (4)

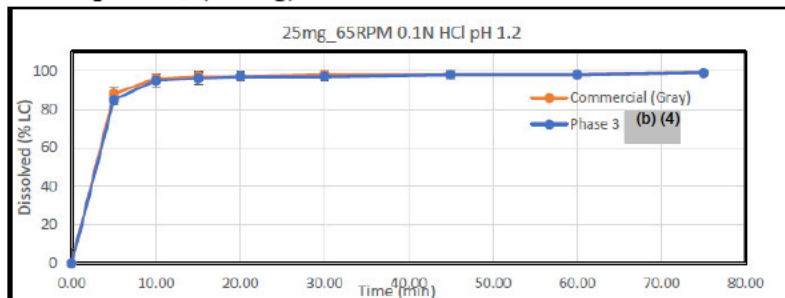
(b) (4) The dissolution studies were conducted to compare the dissolution profiles of Phase 2 with Phase 3 and Phase 3 with commercial drug product at pHs of 1, 2, 4.5, and 6.8 using the USP Apparatus II at paddle speeds of 65 rpm and 500 mL of the dissolution media. Dissolution data in pH 1.2 (QC) media showed very rapid drug release from the formulations. Based on the totality of the information, the Applicant adequately bridged between the phase 3 and commercial formulations.

Table 4: The Batch Information of Phase 3 and Commercial Tablets (25 mg)

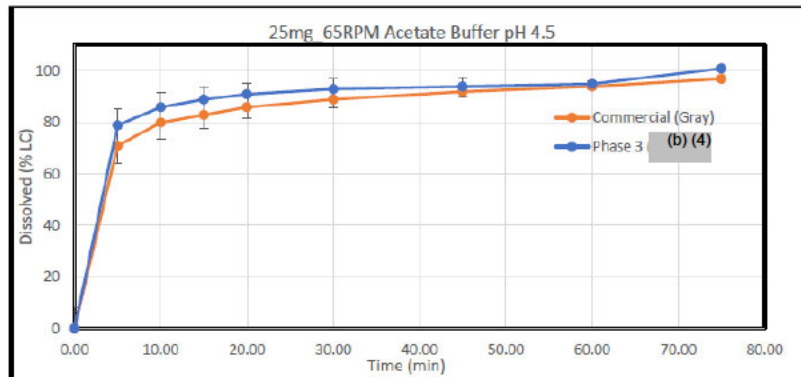
	Phase 3 (b) (4)	Mfg Date	De-bossed Gray (b) (4)	Mfg Date
Batch No. (Batch Size)	CMFCP (b) (4) kg	July 09, 2022	CMDGZ (b) (4) kg	July 8, 2022
	CNNXF (b) (4) kg	October 6, 2023	CPSDP (b) (4) kg	July 10, 2023
Manufacturer	Patheon-Whitby, Ontario, Canada			
Use of Batch	Development		Development	

Figure 16: Comparison Between Phase 3 and Commercial Tablets

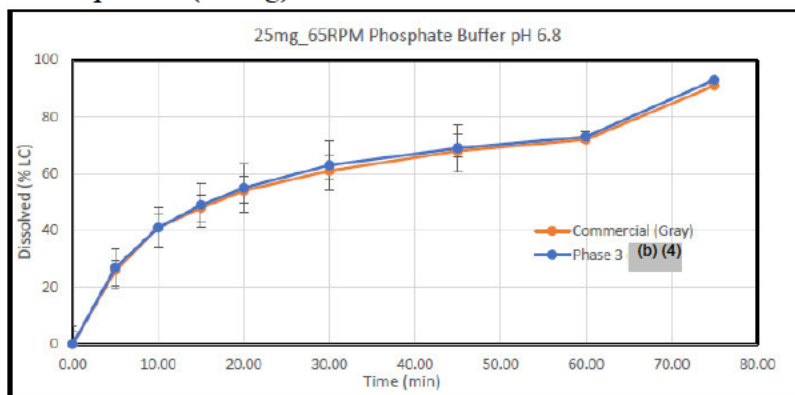
a. pH 1.2, (25 mg)



b. pH 4.5 (25 mg)



c. pH 6.8 (25 mg)



Appendix 1. Dissolution Data

Dissolution data:

1. <\\CDSESUB1\EVSPROD\nda217673\0016\m1\us\attach-1-25mg-dissolution.pdf>
2. <\\CDSESUB1\EVSPROD\nda217673\0016\m1\us\attach-2-10mg-dissolution.pdf>

Appendix 2. Information request

(b) (4)

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Ghosh

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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	217673
Assessment Cycle Number	1
Drug Product Name	BRINSUPRI

Assessment Recommendation: Choose an item.

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Inadequate	N/A
Patient Information	Inadequate	N/A
Instruction for Use (IFU)	Adequate	24, 01
Container Labels	Inadequate	N/A
Carton Labeling	N/A	N/A

Brief Description of Outstanding Issues:

List inactive ingredients in alphabetical order, include the street address for the Applicant's address (in addition to city, state, and ZIP code), define acronyms, include more drug substance solubility information, describe the DP and containers in more detail, and clarify the container label.

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
SDN 24, eCTD 24	2025 APR 04	Container label for 10 mg strength DP, prescribing information, patient information, instruction for use.
SDN 1, eCTD 1	2024 DEC 12	Container label for 25 mg strength DP, prescribing information, patient information, instruction for use.



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(b) (4)

End Applicant Material

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 Highlights² [21 CFR 201.57(a)(2)]		
Established name(s) ³	Adequate	BRINSUPRI™ (brensocatib) tablets, for oral use.
Route(s) of administration	Adequate	Oral.
Controlled drug substance symbol (if applicable)	N/A	
Initial U.S. Approval [§201.57(a)(3)]	Adequate	"YYYY" used by Applicant as a placeholder. Brensocatib has not been approved yet, so the year is pending.

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)

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).



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Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		
Dosage form(s) ⁴ and strength(s) in metric system ⁵	Adequate	Both strengths listed in milligrams.
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	
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*

Complies with requirements. The initial U.S. approval year should be updated from “YYYY” as soon as possible.

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>



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(b) (4)

End Applicant Material

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	
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	Instructions detail that administration can occur with or without food.

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](#)



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For parenteral products: include statement: <i>"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."</i> 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 <i>"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures."</i> ^x with x numerical citation to "OSHA Hazardous Drugs."	N/A	

Assessment: Adequate

(b) (4)

End Applicant Material

¹¹ §201.57(c)(3)(iv)

¹² USP General Notices 2.30 Legal Recognition

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)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	Film-coated tablet.
Strength(s) in metric system	Adequate	25 mg and 10 mg.
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	Gray or brown, round, film-coated tablets debossed with "25" or "10", respectively, on one side and "BRE" on the other.
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	

Assessment: Adequate



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End Applicant Material

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



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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	The API name is brensocatib.
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	Tablets are available 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 of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].	N/A	
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)].	Inadequate	The listed inactive ingredients should be reorganized into 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	

¹⁵ Use of "USP" descriptor is not required to be included next to the established name throughout Prescribing Information (PI) labeling. If an applicant wants to use the "USP" descriptor next to the established name in the PI, recommend limiting its use to the product quality sections of the Full Prescribing Information (FPI) (i.e., DOSAGE FORMS AND STRENGTHS, DESCRIPTION, HOW SUPPLIED/STORAGE AND HANDLING) (see page 3 of LRT).

¹⁶ Per § 201.100(b)(5)(i) and (ii), flavoring and colorants may be designated as such without naming their components except for FD&C Yellow No 5 and FD&C Yellow No 6, which must be listed per § 201.20. Per § 201.100(b)(5)(iii), trace amounts of harmless substances added solely for individual product identification need not be named. If an applicant wants to use the National Formulary (NF) descriptor next to excipients, recommend limiting its use to the product quality sections of the FPI (see page 3 of LRT). Do not list brand names, e.g., Opadry, Eudragit, Polistirex, etc.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
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	DPP1 inhibitor.
Chemical name ¹⁸ , structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	N/A	
For oral prescription drug products, include gluten statement ¹⁹ (if applicable).	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity").	Adequate	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

¹⁷ Listed before "indicated for" in INDICATIONS AND USAGE of Highlights section [§ 201.57(a)(6)]; can also search the term "FDA EPC Text Phrases" in [FDA's Labeling Resources for Human Prescription Drugs](#) for the most recent EPC list.

¹⁸ Chemical names do not need to be capitalized unless it appears at the beginning of a sentence (see *Preferred IUPAC Names Provisional Recommendation*, September 2004; Chapter 1, par. 16 Name writing, p.80-90).

¹⁹ Draft guidance: [Gluten in Drug Products and Associated Labeling Recommendations \(December 2017\)](#)

Assessment: Inadequate

The following were found inadequate in this section:

- In the first sentence in this section, the Applicant should remove (b) (4) and write out the acronym "DPP1".
- In the first paragraph after the structure, more specific information about the solubility profile should be included, such as "brensocatib is soluble at pH ## and insoluble at pH ##". The solubility in other solvents, such as ethanol, should also be described.
- The inactive ingredients should be listed in alphabetical order.

(b) (4)

End Applicant Material

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	Tablets.
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	Two strengths: 25 mg and 10 mg.

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

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)
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	Bottles of 30 tablets for both strengths.
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	Gray or brown, round, film-coated tablets debossed with "25" or "10" on one side for the 25 or 10 mg strength, respectively, and "BRE" on the other side.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	The tablet at both strengths is not scored.
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	
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	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	20°C to 25°C, excursions permitted between 15°C to 30°C.

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)
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	

(b) (4)

Assessment: Inadequate

For the last sentence in the two paragraphs describing the product, change to the following: *and "bre" on the other side. The tablets are stored in 30-count HDPE bottles*

(b) (4)

(b) (4)

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	The Applicant did not include a street address.

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)

(b) (4)



Title:	NDA IQA Template CHAPTER IV-LABELING		
Document ID:	OPQ-ALL-TEM-0045		
Effective Date:	18 Sep 2023	Revision:	00
Total Pages:	19		



Template Revision: 03

Assessment: Inadequate

The Applicant's address included the city, state, and ZIP code, but did not include the street.

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	
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.	N/A	
Active ingredient(s) (if applicable).	Adequate	
Alphabetical listing of inactive ingredients (if applicable).	Inadequate	The listed inactive ingredients should be reorganized into alphabetical order.
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Inadequate	The Applicant did not include a street address.

Assessment: Inadequate

The inactive ingredients should be listed in alphabetical order and the Applicant's address included the city, state, and ZIP code, but did not include the street.

3.0 CONTAINER AND CARTON LABELING²⁵

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

²⁵ [Carton and Container Labeling Resources](#)



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Template Revision: 03

3.1 Container Labels²⁶

Start Applicant Material

Draft Bottle Label 25 mg

Note: red dash lines are for printing purposes and do not show on the label

(b) (4)

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.

Draft Bottle Label 10 mg

Note: red dash lines are for printing purposes and do not show on the label



3.2 Carton Labeling

N/A. No carton information nor mentioning of carton usage was included in this application.

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.	
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.	The month format is MMM, corresponding to the first three letters of the month.
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.	The name and address of the drug product manufacturer is absent, but the distributor information is present.
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	Adequate	Choose an item.	The Applicant included this statement even though it is optional for Rx.
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: *Inadequate*

“Product of Spain” should be removed from the container label. The container labels should include the name and address (street, city, and ZIP code) of the manufacturer.

Note: The Applicant did not have an outer carton or additional container. The only container for the commercial drug product is the HDPE bottle.

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

PI 1.2.3 Section 11 (DESCRIPTION): The following were found inadequate in this section:

- In the first sentence in this section, the Applicant should remove (b) (4) and write out the acronym “DPP1”.
- In the first paragraph after the structure, more specific information about the solubility profile should be included, such as “brensocatib is soluble at pH #.# and insoluble at pH #.#”. The solubility in other solvents, such as alcohol, should also be described.
- The inactive ingredients should be listed in alphabetical order.

PI 1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING): For the last sentence in the two paragraphs describing the product, change to the following: *and “bre” on the other side. The tablets are stored in 30-count HDPE bottles* (b) (4)

2.0 PATIENT LABELING: The inactive ingredients should be listed in alphabetical order and the Applicant’s address included the city, state, and ZIP code, but did not include the street.

3.1 Container Labels: “Product of Spain” should be removed from the container label. The container labels should include the name and address (street, city, state, country if foreign, and ZIP code) of the manufacturer.

Primary Labeling Assessor Name and Date:

AUSTIN YU (2025 MAY 01)

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

JULIA PINTO (2025 MAY 01)



Austin
Yu

Digitally signed by Austin Yu

Date: 5/01/2025 12:11:04PM

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Julia
Pinto

Digitally signed by Julia Pinto

Date: 5/01/2025 12:55:19PM

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Craig
Bertha

Digitally signed by Craig Bertha

Date: 5/09/2025 08:14:53AM

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CRAIG M BERTHA
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