CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219972Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number	219972		
Applicant Name	Bayer HealthCare Pharmaceuticals Inc.		
Drug Product Name	HYRNUO™ (sevabertinib) tablets		
Dosage Form	Tablet		
Proposed Strength(s)	10 mg		
NDA Classification	Type 1 - NME		
Route of Administration	Oral		
Maximum Daily Dose	40 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	HYRNUO is indicated for the treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung cancer whose tumors have HER2 (ERBB2) tyrosine kinase domain activating mutations, as detected by an FDA-approved test.		
Drug Product Description	HYRNUO™ (sevabertinib) tablets are presented as red brown film-coated, round, biconvex tablets debossed with “SE” on one side and “10” on the other side.		
Co-packaged product information	N/A		
Device information	N/A		
Storage Temperature/ Conditions	20°C to 25°C		
Review Team	**Discipline**	**Primary**	**Secondary**

	Drug Substance	Rishi Paudel, Ph.D.	Karina M. Zuck, Ph.D.
	Drug Product/ Labeling	Olen Stephens, Ph.D.	Yang Nan, Ph.D./David Claffey, Ph.D.
	Manufacturing	David Acevedo, Ph.D.	Nathan Davis, Ph.D.
	Biopharmaceutics	Rushikesh Sable, Ph.D.	Hardikkumar Patel, Ph.D.
	Microbiology	-	-
	Other (specify)	-	-
	RBPM	Dahlia Walters, Pharm.D.	
	ATL	Yang Nan, Ph.D.	
Consults	None		

2. Final Overall Recommendation - *APPROVAL*

3. Action Letter Information

a. Expiration Dating:

Based on the stability data submitted to date, an expiry dating period of 24 months for HYRNUO™ (sevabertinib) tablets may be granted when stored 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].

b. Additional Comments for Action:

None

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

Based on our evaluation of the available information, the Applicant has provided sufficient data to support an approval recommendation from the drug product quality perspective. The submission includes adequate information to ensure the identity, strength, purity, and quality of HYRNUO™ (sevabertinib) tablets. Manufacturing inspections of all associated facilities support an approval recommendation. The proposed labeling meets regulatory requirements.

OPQ recommends APPROVAL of NDA 219972 for the commercialization of HYRNUO™ (sevabertinib) tablets, 10 mg.

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

Recommendation by Subdiscipline:

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

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

5. Life-Cycle Considerations

Established Conditions per ICH Q12: Yes

Comments: The applicant will be alerted through an information request for the cross-referenced IND that, as the lifecycle control for this product, if non-ICH S9 indications are sought, a new risk assessment should be conducted. See the drug product quality review for more details.

Comparability Protocols (PACMP): No

Additional Lifecycle Comments: None

Application Technical Lead Name and Date: *Yang Nan, Ph.D., October 21, 2025*

Yang Nan

Digitally signed by Yang Nan
Date: 10/21/2025 12:52:27PM
GUID: 520bd6c90002b3b0320380334e69a817

CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information: The label is adequate as currently written in the clinical division's SharePoint site. Labeling negotiations are on-going at the time of this review. The information captured below represents the edits made at the time of this review.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Items in Proposed Labeling	Assessor's Comments
Product Title in Highlights		
Established name(s)[1]	Adequate	HYRNUO® (sevabertinib) tablets
Route(s) of administration	Adequate	for oral use
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Adequate	Tablets: 10 mg '*of sevabertinib*'
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 parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	
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).	N/A	

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

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Items in Proposed Labeling	Assessor's Comments
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)	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	Swallow tablets whole. Do not cut, crush, or chew the tablets
For parenteral products: include statement: *"Parenteral drug products must be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit"*	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 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s)	N/A	

who administer the drug		
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	

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Items in Proposed Labeling	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	Tablets
Strength(s) in metric system	Adequate	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 (Tablets: 10 mg of drug-x hydrochloride).	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	red brown film-coated, round, biconvex tablets debossed with "SE" on one side and "10" on the other side '*containing 10 mg of sevabertinib*'
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 parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	N/A	

Section 11 (DESCRIPTION)

Item	Items in Proposed Labeling	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	Adequate	HYRNUO tablets
Dosage form(s) and route(s) of administration	Adequate	tablets are 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)"	Adequate	'*Sevabertinib is present as a non-stoichiometric hydrate as'* a white to off-white to yellow to pinkish powder
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	Adequate	The inactive ingredients are: cellulose microcrystalline, crospovidone, lactose monohydrate, and magnesium stearate. The tablet film coating contains ferric oxide red, hypromellose 5 cP, and macrogol 3350.
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.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Sterility statement (if applicable)	N/A	
Pharmacological/Therapeutic class	Adequate	kinase inhibitor
Chemical name, structural formula, molecular weight	Adequate	3-(3-chloro-2-methoxyanilino)-2-{3-[(2S)-1,4-dioxan-2-ylmethoxy]pyridin-4-yl}-1,5,6,7-tetrahydro-4H-pyrrolo[3,2-c]pyridin-4-one hydrate $C_{24}H_{25}ClN_4O_5$ (anhydrate) and the molecular weight is 484.93 g/mol (anhydrate)

If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Adequate	'*Sevabertinib is present as a non-stoichiometric hydrate as'* a white to off-white to yellow to pinkish powder It is slightly soluble in aqueous solution at pH 2, and practically insoluble in aqueous solutions at pH 4.5 and above.

Section 11 (DESCRIPTION) Continued

Item	Items in Proposed Labeling	Assessor's Comments
For oral prescription drug products, include gluten statement (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	

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Items in Proposed Labeling	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Adequate	tablets
Strength(s) in metric system	Adequate	10 mg
Available units (e.g., bottles of 100 tablets)	Adequate	bottle of 120 tablets
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	Adequate	red brown film-coated, round, biconvex tablets debossed with "SE" on one side and "10" 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	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	
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."	N/A	

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Items in Proposed Labeling	Assessor's Comments
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Adequate	Store at 20°C to 25°C (68°F to 77°F); excursions permitted between (b) (4) to 30°C ((b) (4) to 86°F) [see USP Controlled Room Temperature].
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*	N/A	
Include information about child-resistant packaging	Adequate	packaged in a HDPE bottle of 120 tablets closed with a child-resistant screw cap

1.2.5 Other Sections of Labeling

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Items in Proposed Labeling	Assessor's Comments
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer	Adequate	Manufactured for: Bayer HealthCare Pharmaceuticals Inc. Whippany, NJ 07981

2.0 PATIENT LABELING

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

Item	Items in Proposed Labeling	Assessor's Comments about Carton Labeling
Established name[2]	Adequate	HYRNUO® (sevabertinib) tablets
Special preparation instructions (if applicable)	N/A	
Storage and handling information (if applicable)	Adequate	Store HYRNUO at room temperature between 68°F to 77°F (20°C to 25°C)
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differs from the dosage form.	N/A	
Active ingredient(s) (if applicable)	Adequate	Active ingredient: sevabertinib
Alphabetical listing of inactive ingredients (if applicable)	Adequate	Inactive ingredients: cellulose microcrystalline, crospovidone, lactose monohydrate, and magnesium stearate. Tablet film coating: ferric oxide red, hypromellose 5 cP, and macrogol 3350
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer	Adequate	Manufactured for: Bayer HealthCare Pharmaceuticals Inc., Whippany, NJ 07981 USA

3.0 CONTAINER AND CARTON LABELING

3.1 Container Labels

(b) (4)

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

3.2 Carton Labeling

Item	Items in Proposed Labeling	Assessor's Comments about Carton Labeling
Established name[3], (font size and prominence)	Adequate	
Strength(s) in metric system	Adequate	10 mg
Route(s) of administration	Adequate	'Oral use' on carton; not enough room on container for additional information.
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	N/A	
Net contents (e.g., tablet count, volume of liquid)	Adequate	120 film-coated tablets
"Rx only" displayed on the principal display	Adequate	
NDC	Adequate	NDC 50419-397-01
Lot number and expiration date	Adequate	Space provided
Storage conditions. If applicable,	Adequate	'Storage: Store at 20°C to 25°C

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

include a space on the carton labeling for the user to write the new beyond-use-date (BUD).		(68°F to 77°F); excursions permitted between (b) (4) to 30°C ((b) (4) to 86°F) [see USP Controlled Room Temperature]. **Keep out of reach of children**
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement.	N/A	
For parenteral injectable dosage forms, include the name and quantities of all active and inactive ingredients in alphabetical order. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Linear Bar code	Adequate	Present

Item	Items in Proposed Labeling	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor /packer	Adequate	Manufactured for: Bayer HealthCare Pharmaceuticals Inc., Whippany, NJ 07981 USA
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	
No text on Ferrule and Cap overseal, unless a cautionary statement is required.	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	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	N/A	

relevant compendium, its difference shall be plainly stated on its label.		
And others, if space is available.	Adequate	Manufactured in Germany

Assessment of Carton and Container Labeling: Adequate

ITEMS FOR ADDITIONAL ASSESSMENT

None

Overall Assessment and Recommendation:

The label is adequate as currently written in the clinical division's SharePoint site. Labeling negotiations are on-going at the time of this review. The information captured above represents the edits made at the time of this review. Note that the primary and secondary containers include a graphic prior to the proprietary name that could be confusing or distracting. An information request was coordinated with DMEPA to remove this graphic, but the response is pending.

Primary Labeling Assessor Name and Date: Olen Stephens 9/5/2025

Secondary Assessor Name and Date: David Claffey 9/5/2025

Olen Stephens

Digitally signed by Olen Stephens
Date: 9/05/2025 09:29:41AM
GUID: 508da71e00029e680c3cf42984dfa0ee
Comments: The clinical labeling meeting was held for the CMC sections and no significant changes were made related to the CMC section.

David Claffey

Digitally signed by David Claffey
Date: 9/05/2025 03:34:15PM
GUID: 508da71e00029e20b201195abff380c2

CHAPTER VI: BIOPHARMACEUTICS

NDA Number	NDA 219972
Application type	505(b)(1)
Assessment Cycle Number	1 (Original NDA)
Drug Product Name/ Strength	Sevabertinib Tablets 10 mg
Route of Administration	Oral
Applicant Name	Bayer Healthcare Pharma
Therapeutic Classification/ OND Division	Anti-Cancer Division of Oncology 2 (DO2)
Proposed Indication	For the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) harboring HER2 mutations

Assessment Recommendation: Adequate.

Assessment Summary:
The Applicant Bayer Healthcare Pharma. is seeking approval of NDA 219972 for Sevabertinib Tablets10 mg under 505(b)(1) regulatory pathway. Sevabertinib is a New Molecular Entity (NME) targeting HER2-mutant non-small cell lung cancer (NSCLC). Sevabertinib exhibits the characteristics of a BCS-II (low solubility, high permeability) drug substance. The proposed drug product exhibits rapid dissolution at pH1.2 however, at pH 4.5 and pH 6.8 it demonstrated comparatively slower and incomplete release.

Review Objective: The focus of the current Biopharmaceutics review is to assess the dissolution method, drug release specifications for the proposed drug product quality control (QC) and the scientific bridging of the clinical formulation to the proposed commercial formulation.

Recommendation: Based on the totality of data/information provided, the following dissolution testing method and acceptance criterion are approved for the QC of the proposed drug product at batch release and throughout the stability program/shelf-life.

Final Dissolution Method and Acceptance Criterion:

Apparatus Type	Rotation Speed	Medium/ Volume	Temperature	Acceptance Criterion
USP apparatus II (Paddle)	50 rpm	Phosphate buffer pH 6.8 + 0.3% SDS / 900 mL	37.0 ± 0.5 °C	Q= (b) (4) in 30 Minutes

Bridging: Applicant submitted comparable dissolution profiles of representative batches from (b) (4) process to bridge the (b) (4) changes made during the development phase and to be marketed drug product. Dissolution profiles of representative batches from (b) (4) process demonstrated comparable dissolution behavior in QC method. All batches exhibit more than (b) (4) release in 30 min.

Biowaiver: The Applicant has proposed only one strength (Sevabertinib Tablets, 10 mg). Biowaiver is neither requested nor needed.

Overall recommendation: From a Biopharmaceutics perspective, NDA 219972 for Sevabertinib Tablets, 10 mg is recommended for APPROVAL.

CQAs	Initial Risk Ranking	Comments	Updated Risk Ranking	Comments
Drug substance particle size	Medium	Low Solubility: Drug substance particle size may impact drug product dissolution	Low	(b) (4)

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
SN -1 (original NDA)	03/28/2025
SN- 19 (Response to Biopharmaceutics IR)	07/03/2025
SN- 31 (Response to Biopharmaceutics IR)	08/08/2025
SN- 49 (Response to Biopharmaceutics IR)	09/30/2025

Concise Description of Outstanding Issues: Not Applicable

B.1 BCS DESIGNATION

Assessment: Not applicable

There is no official BCS designation request for the proposed drug product.

Solubility: Based on the provided solubility data, the drug substance exhibits pH dependent solubility, specifically the data shows Sevabertinib has high solubility at acidic pH (pH 1.0 and 2.0), and solubility decreases as pH increases (pH 4.5 and 6.8).

Table 1. Saturation solubility of Sevabertinib (37 °C)

Medium		mg/mL at 37°C /24h	Highest dose (10 mg)/solubility volume (mL)
Buffer	Surfactant		
0.1 M HCl pH 1.0			(b) (4)
0.01 M HCl pH 2.0			
Acetate buffer pH 4.5			
Acetate buffer pH 4.5			
Acetate buffer pH 4.5			
Phosphate buffer pH 6.8			
Phosphate buffer pH 6.8			
Phosphate buffer pH 6.8			
Phosphate buffer pH 6.8			

Sevabertinib exists in three crystalline polymorphic forms: (b) (4) (b) (4) has been selected as the target polymorphic form for commercial manufacturing and is controlled in the drug substance specification. During stability studies of sevabertinib tablets 10 mg, (b) (4) (b) (4) was observed in some batches. The (b) (4) (b) (4) exhibits slightly higher solubility over the physiological pH range compared to the target (b) (4).

(b) (4)

In vitro dissolution experiments demonstrate[1] that the batch manufactured with (b) (4) (batch no. 18B-220816-404) showed faster dissolution compared to batches manufactured with (b) (4) (batch nos. 18B-220725-402, KM603NA, KM60481) across physiological pH conditions (pH 1.2-6.8). Based on exposure-response analysis from clinical studies, Clinical reviewer confirmed that the absorption rate constant was not identified as a statistically significant covariate in the exposure response (ER) analysis for either safety or efficacy when compared tablets vs oral solution formulation (worst-case scenario with a complete change). Therfore, (b) (4) would not affect the safety and efficacy of the drug product.

Permeability: The Applicant claims high permeability for Sevabertinib based on the results of *in vitro* Caco-2 data.

Dissolution: The proposed drug product exhibits rapid dissolution at pH 1.2 and demonstrated incomplete release at pH conditions 4.5 and 6.8 without the use of any surfactant.

B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA

Assessment: *Adequate*

Dissolution Method:

In the original application[2] the Applicant proposed the following quality control dissolution method and acceptance criterion for Sevabertinib Tablets, 10 mg:

Apparatus	Speed	Medium	Volume/ Temperature	Acceptance Criterion
USP Apparatus II (Paddle)	50 rpm	Phosphate buffer pH 6.8 + (b) (4) SDS	900 mL/ 37 ± 0.5 °C	Q= (b) (4) in 30 minutes

[1] \\CDSESUB1\EVSPROD\nda219972\0001\m3\32-body-data\32p-drug-prod\bay-2927088-coated-tablet-10-mg-bayer-ag\32p2-pharm-dev\additional-information-022992016.pdf

[2] \\CDSESUB1\EVSPROD\nda219972\0001\m3\32-body-data\32p-drug-prod\bay-2927088-coated-tablet-10-mg-bayer-ag\32p2-pharm-dev\dissolution-profiles-022990249.pdf

The Applicant conducted evaluation of the dissolution profile for the proposed drug product, Sevabertinib Tablets, 10 mg, across a range of physiological pH conditions. The assessment covered various dissolution parameters, including apparatus types (USP (b) (4) II), agitation speed, media volume, and concentration of surfactant. Based on the observed gradual release pattern and complete release relative to other pH conditions, the Applicant initially proposed a dissolution method utilizing a phosphate buffer pH 6.8 + (b) (4) SDS as a dissolution medium.

Figure 1: (b) (4)

Figure 2:

Based on the provided dissolution, via Information Request (IR dated 06/04/2025) the Applicant was informed that the proposed dissolution method lacks adequate justification to demonstrate the discriminating ability towards meaningful changes in the critical bioavailability attributes (CBAs) which includes the influence of particle size distribution, (b) (4), accelerated stability testing and (b) (4). Therefore, agency recommended to Applicant to develop a dissolution method suitable for the proposed product with adequate justification and supporting data for selected dissolution conditions.

To justify the discriminating ability of dissolution method, in response to the IR[3] the Applicant provided dissolution data for batches manufactured with different (b) (4) sizes (b) (4). The dissolution method [900 mL of phosphate buffer pH 6.8 + (b) (4) SDS, 50 rpm, Paddle Apparatus] demonstrated discriminating ability towards meaningful changes in the (b) (4) size.

Figure 3 (b) (4)

Additionally, the Applicant provided dissolution data for more concentrations of SDS with phosphate buffer pH 6.8 as a dissolution medium.

[3] \\CDSESUB1\EVSPROD\nda219972\0019\m3\32-body-data\32p-drug-prod\bay-2927088-coated-tablet-10-mg-bayer-ag\32p5-contr-drug-prod\32p53-val-analyt-proc\method-development-dissolution-iqms-383198.pdf

Figure 4 

The dissolution profile data using (b) (4) SDS or 0.3% SDS in phosphate buffer pH 6.8 were comparable, with complete drug release achieved under both conditions for the proposed drug product. Based on the dissolution profiles, a (b) (4) concentration of surfactant in the dissolution medium was not justified. Therefore, upon review of the dissolution method development information and data submitted on 07/03/2025 and 08/08/2025, FDA recommended, and the Applicant subsequently accepted, the QC dissolution method [USP Apparatus II (Paddle), 50 rpm, 900 mL of phosphate buffer pH 6.8 + 0.3 % SDS, 37.0 ± 0.5°C] for Sevabertinib Tablets, 10 mg.

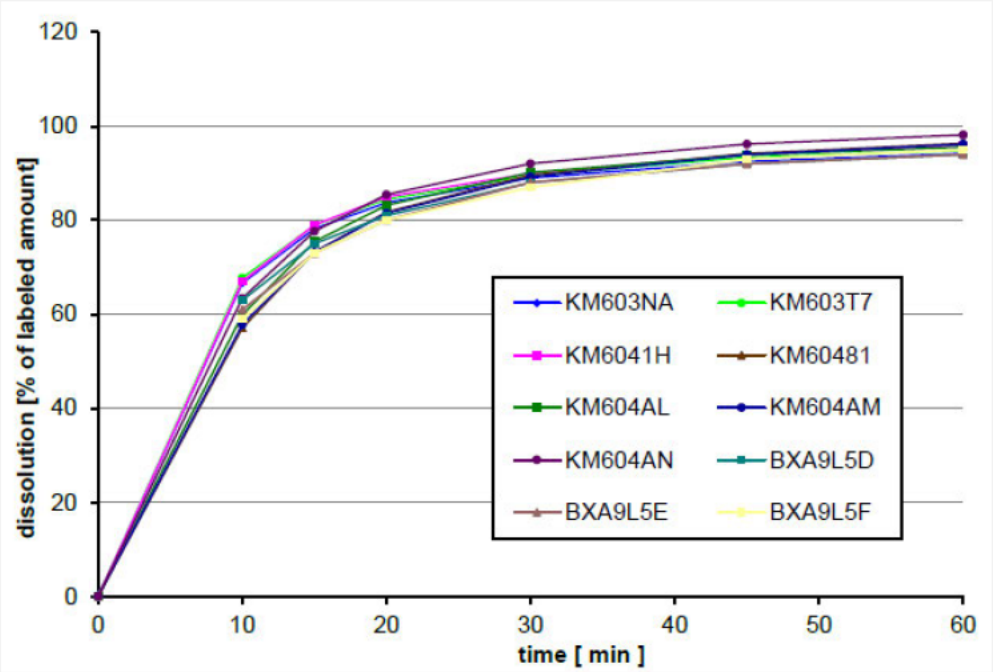
Dissolution data:

Dissolution profiles of representative batches from (b) (4) process demonstrated comparable dissolution behavior in QC method. All batches exhibit more than (b) (4) release in 30 min.

Table 3: Mean dissolution results of representative batches from (b) (4) process, QC conditions (n=12)

Batch	Use of batch	Mean % Dissolved at Sampling time [min]					
		10	15	20	30	45	60
Batches produced by (b) (4) Process							
KM603NA	Clinical	67	78	84	89	93	94
KM603T7	Clinical	68	79	85	90	93	95
KM6041H	Clinical	67	79	85	90	94	96
Batches produced by (b) (4) Process							
KM60481	Clinical	57	73	82	90	94	96
KM604AL	Primary stab./Clinical	60	75	83	90	94	96
KM604AM	Primary stab./Clinical	58	73	82	89	94	96
KM604AN	Primary stab./Clinical	63	78	85	92	96	98
BXA9L5D	Process Validation	63	75	81	88	92	94
BXA9L5E	Process Validation	61	73	80	88	92	94
BXA9L5F	Process Validation	59	73	80	87	93	95

Figure 5. Mean Dissolution Profiles of representative batches from (b) (4) process in QC method [900 mL of pH 6.8 phosphate buffer with 0.3% SDS, USP- II Paddle, 50 rpm].



Dissolution Acceptance Criteria:

Based on the similar comparable dissolution profiles of originally proposed dissolution method and revised dissolution method; Applicant's initially proposed an acceptance criterion of "Q= (b) (4) in 30 minutes" was found to be acceptable.

Based on the overall dissolution method development data and the clinical data provided, the following dissolution method and acceptance criterion is approved for the QC of the proposed drug product at batch release and stability specifications:

Final Approved Dissolution Method Acceptance Criterion:

Apparatus Type	Rotation Speed	Medium/ Volume	Temperature	Acceptance Criterion
USP apparatus II (Paddle)	50 rpm	Phosphate buffer pH 6.8 + 0.3% SDS / 900 mL	37.0 ± 0.5 °C	Q= (b) (4) in 30 minutes

Stability Testing:
In accelerated stability testing for some drug product registration batches, a (b) (4) (b) (4) was observed. Based on the data of exposure-response analysis clinical study; the Applicant claimed that that even if there was a (b) (4) safety and efficacy of the drug product would not be affected (which is reviewed by the OCP). The Applicant submitted dissolution data for the batches made with (b) (4) Sevabertinib which found to be comparable which mitigates the risk to low.

B.12 BRIDGING OF FORMULATIONS

Assessment: *Adequate*

To bridge any minor changes between clinical and to-be-marketed commercial batches, including changes (b) (4), the Applicant submitted comparative dissolution profile data using the revised dissolution method. All representative batches from (b) (4) process demonstrated comparable dissolution profiles with f2 similarity factor values more than 50 [4].

B. 13 BIOWAIVER REQUEST

Assessment: *Not Applicable*

There is only one strength (10 mg) proposed for marketing, and this strength was evaluated in the pivotal clinical trial (as well as in registration/stability studies).

[4] \\CDSESUB1\EVSPROD\nda219972\0049\m3\32-body-data\32p-drug-prod\bay-2927088-coated-tablet-10-mg-bayer-ag\32p2-pharm-dev\dissolution-profiles-iqms-383196.pdf

R. REGIONAL INFORMATION

Comparability Protocols

None

Post-Approval Commitments

None

Lifecycle Management Considerations

None

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None

Primary Biopharmaceutics Assessor's Name and Date:
Rushikesh Sable, Ph.D.

Secondary Assessor Name and Date (and Secondary Summary, as needed):
Hardikkumar Patel, Ph.D.

(b) (4)

Rushikesh Sable

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Hardikkumar Patel

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Date: 10/02/2025 03:11:40PM
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