CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219293Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number.	219293
Applicant Name	Slayback Pharma LLC
Drug Product Name	DANZITEN (nilotinib) Tablets
Dosage Form.	Tablet
Proposed Strength(s)	71 mg and 95 mg
Route of Administration	Oral
Maximum Daily Dose	380 mg
Rx/OTC Dispensed	Rx
Proposed Indication	DANZITEN is a kinase inhibitor indicated for the treatment of: • Adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase. • Adult patients with chronic phase (CP) and accelerated phase (AP) Ph+ CML resistant to or intolerant to prior therapy that included imatinib.
Drug Product Description	The proposed drug product is an immediate release, coated, debossed tablets and is available in two strengths i.e., 71 mg and 95 mg. The two strengths are (b) (4) appropriately differentiated by their coating color and debossing. Nilotinib tablets are packaged in clear (b) (4) blister pack with (b) (4) .
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 to 15°C to 30°C (59°F to 86°F), USP controlled room temprature conditions.		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Rajan Pragani	Haripada Sarker
	Drug Product/ Labeling	Xiao Hong	Shalini Anand
	Manufacturing	Diane Goll	Zhaoyang Meng
	Biopharmaceutics	Hardik Patel	Anitha Govada
	Other (specify):	N/A	N/A
	RBPM	Dahlia Walters	
	ATL	Shalini Anand	
Consults	N/A		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: An expiration dating period of **24 months** is granted for the drug product when stored at USP controlled room temprature storage conditions i.e., 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F).

b. Additional Comments for Action: n/a

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4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

OPQ recommends ***APPROVAL*** of NDA 219293 for the commercialization of DANZITEN (nilotinib) 71 mg and 95 mg tablets. Based on our evaluation of the available information, the Applicant provided sufficient information to support an approval recommendation from the drug product quality perspective. The Applicant provided adequate information on the proposed drug product to ensure the identity, strength, purity, and quality of the proposed drug product. The overall manufacturing inspection recommendation is approval for all the facilities associated with this application. The proposed labeling and labels include adequate information to meet the regulatory requirements.

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: No
Comments:

Comparability Protocols (PACMP): No

Comments: N/A

Additional Lifecycle Comments: N/A

Shalini Anand

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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	219293
Assessment Cycle Number	1
Drug Product Name	Nilotinib

Assessment Recommendation: Adequate

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Adequate	**#0001**
Patient Information	Adequate	**#0001**
Instruction for Use (IFU)	N/A	**NA**
Container Labels	Adequate	**#0001**
Carton Labeling	Adequate	**#0001**

Brief Description of Outstanding Issues: N/A

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
#0001	01/30/2024	PI and container carton labels
#0016	09/09/2024	Labeling

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

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

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights[2] [21 CFR 201.57(a)(2)]		
Established name(s)[3]	Adequate	DANZITEN (nilotinib) tablets
Route(s) of administration	Adequate	For oral use
Controlled drug substance symbol (if applicable)	N/A	
Initial U.S. Approval [§201.57(a)(3)]	Adequate	Initial U.S. Approval: 2007
Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		
Dosage form(s)[4] and strength(s) in metric system[5]	Adequate	Tablets: 71 mg and 95 mg
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).[6]	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	N/A	

[2] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018)
[3] Established name = [Drug] [Route of Administration] [Dosage Form]. Do use not "USP" descriptor in the product title or within the Highlights (see page 3 of LRT).
[4] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018); USP <1151>; USP Nomenclature Guideline
[5] Labeling Review Tool (March 2022, page 13), include limited packaging information; USP <7>
[6] Guidance: *Naming of Drug Products Containing Salt Drug Substances* (June 2015); MAPP 5021.1
[7] Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (March 2013)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.[8]	N/A	

Assessment: *Adequate*

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

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(*copy of proposed text*)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents and/or soft food[10], storage conditions needed to maintain the stability of the reconstituted or diluted product).	N/A	

[8] Guidance: *Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use* (October 2018); USP <659>

[9] See § 201.57(c)(3); draft guidance: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023); Labeling Review Tool (March 2022, page 25)

[10] Draft Guidance: Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	
For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11]	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]"* with x numerical citation to "OSHA Hazardous Drugs."	N/A	

Assessment: *Adequate*

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

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

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

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	Tablets
Strength(s) in metric system	Adequate	(b) (4) mg and (b) (4) 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.	Adequate	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable.	Adequate	Tablets • 71 mg: pink coated oblong tablets, debossed with "N5" on one side and plain on other side. Each tablet contains 71 mg of nilotinib. • 95 mg: yellow coated oblong tablets, debossed with "N2" on one side and plain on other side. Each tablet contains 95 mg of nilotinib.
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	N/A	

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

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

Assessment: *Adequate*

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

1.2.3 Section 11 (DESCRIPTION)[14]

(b) (4)

[redacted]

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

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)[15] [§ 201.57(c)(12)(i)(A)].	Adequate	DANZITEN™ (Nilotinib) tablets
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	DANZITEN™ (Nilotinib) tablets, for oral use
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "DANZITEN contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].	Adequate	The descriptions for Nilotinib tablets have been edited to make it more clear as follows: DANZITEN (nilotinib) tablets contain 71 mg or 95 mg nilotinib, equivalent to 91.14 mg, and 121.95 mg nilotinib tartrate, respectively. The inactive ingredients are: colloidal silicon dioxide, croscarmellose sodium, hypromellose acetate succinate, iron oxide red (in 71 mg strength tablets), iron oxide yellow (in 95 mg strength tablets), magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.
List inactive ingredients (not required for oral use, except for colorant) by the USP/NF names in alphabetical order.[16] Avoid brand names. [§ 201.57(c)(12)(i)(C)].	Adequate	All inactive ingredients are listed but not in alphabetical order. The edit has been made so that they are provided in alphabetical order.

[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)
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	Nilotinib is a kinase 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)].	Adequate	Nilotinib tartrate is a white to slightly yellowish powder. The solubility of nilotinib tartrate in aqueous solutions decreases with increasing pH. The pK_a1 was determined to be 3.53; pK_a2 was estimated to be 1.55.
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	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)

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)
Drug Company X," "structurally unique molecular entity").		
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

Assessment: *Adequate*

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

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

(b) (4)

[redacted]

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

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s) [§ 201.57(c)(17)].	Adequate	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	71 mg and 95 mg
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s) [§ 201.57(c)(17)(iii)].	Adequate	DANZITEN (nilotinib) 71 mg tablets are pink, coated, oblong tablets, debossed with "N5" on one side and plain on other side. DANZITEN (nilotinib) 95 mg tablets are yellow, coated, oblong tablets, debossed with "N2" on one side and plain on other side. DANZITEN (nilotinib) 71 mg and 95 mg tablets are supplied in blister packs.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs." [§ 201.57(c)(17)(iv)]	N/A	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	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]*.
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*[21]	N/A	
Include information about child-resistant packaging[22] (if chosen by manufacturer).	Adequate	

[21] Guidance: *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex* (December 2014)
[22] Guidance: *Child-Resistant Packaging Statements in Drug Product Labeling* (August 2019)

Assessment: *Adequate*

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

1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug review division if the product contains any of these inactive ingredients.

Please include your comments about other sections of labeling if they contain product quality information.

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

Item	Item in Proposed Labeling (choose "Adequate" or "Inadequate")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer.	Adequate	Name and location is provided but street address is not listed. A comment has been included to ask the applicant to include street address.

Assessment: *Adequate*

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

2.0 PATIENT LABELING

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

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

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).	Adequate	All inactive ingredients are listed but not in alphabetical order. The applicant is asked to list inactive ingredients in alphabetical order.
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Adequate	

Assessment: *Adequate*

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

3.0 CONTAINER AND CARTON LABELING[25]

3.1 Container Labels[26]

(Copy/paste or refer to a representative example of a proposed container label)

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

[25] Carton and Container Labeling Resources

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

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Proprietary name and established name[27], (font size and prominence) [§ 201.10(g)(2)].	Adequate	Yes	DANZITEN (Nilotinib) tablets
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	Adequate	Yes	71 mg and 95 mg
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	Adequate	Yes	
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP [§ 201.10(d)(1) & 201.100(b)(4), USP <1121>].	Adequate	Yes	The equivalency statement is not provided. IR: Under the DP strength include an equivalency statement between the salt and free base form of the API.
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	Adequate	Yes	28 (1 pack (b) (4)) or 4x28 (4 pack (b) (4)) count for both 71 mg and 95 mg tablets;
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Adequate	Yes	
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	Yes	
Lot number and expiration date [§ 201.18 & 201.17].	Adequate	Yes	
Storage conditions. If applicable, include a space on the carton labeling for the	Adequate	Yes	Store at 20°C to 25°C (68°F to 77°F); excursions

[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)
user to write the beyond-use-date (BUD).			permitted between 15°C to 30°C (59°F to 86°F)
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	Yes	
Adequate directions for use: "Recommended Dosage: See	Adequate	Yes	

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

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Prescribing Information" [§ 201.5 & 201.55].			
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	Yes	
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	Adequate	Yes	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	Choose an item.	
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	N/A	Choose an item.	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	Choose an item.	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.[31]	N/A	Choose an item.	
And others if space is available.	N/A	Choose an item.	

[31] USP General Notices 3.20 Indicating Conformance

Assessment of Carton Labels and Container Labeling: *Adequate*

Any issues should be listed at the end in "OUTSTANDING ISSUES AND RECOMMENDATIONS"

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

Assess consistency of product-quality information in prescription drug labeling (PI, c/c labeling, and FDA-approved patient labeling). See Carton/Container Labeling Specific Resources for a presentation about inappropriate inconsistencies of product quality information between labeling. If there are inappropriate inconsistencies between the labeling (e.g., established name, strength(s), package type term, discard statement, identifying characteristics, storage, reconstitution/dilution instructions), please list these issues in this section.

Primary Labeling Assessor Name and Date: Xiao Hong Chen July 3, 2024

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

Xiao Chen

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David Claffey

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CHAPTER VI: BIOPHARMACEUTICS

Product Information	Tablet/Immediate Release
NDA Number	219293 ORIG-1 [505(b)(2)]
Assessment Cycle Number	1
Drug Product Name/ Strength	Nilotinib Tablets, 71 mg, and 95 mg
Route of Administration	Oral
Applicant Name	Slayback Pharma LLC
Therapeutic Classification/ OND Division	Division of Hematologic Malignancies (DHM1)
LD/Cross referenced NDA	NDA 022068, TASIGNA (Nilotinib) Capsules, 50 mg, 150 mg, and 200 mg EQ Base
Proposed Indication	Philadelphia chromosome positive chronic myeloid leukemia (PH+CML)

Assessment Recommendation: **Adequate**

A. Assessment Summary:

The Applicant, Slayback Pharma LLC., is seeking approval of NDA 219293 for Nilotinib Tablets, 71 mg, and 95 mg under 505 (b)(2) regulatory pathway. The proposed drug product relies on the listed drug, TASIGNA® (nilotinib) Capsules, 50 mg, 150 mg, and 200 mg EQ Base for safety and efficacy of the proposed drug product. The Applicant has provided bioequivalence study data to establish a scientific bridge between the proposed drug product and the LD product.

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

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 stability program/shelf-life.

Final Dissolution Method and Acceptance Criterion:

Apparatus Type	Rotation Speed	Medium/ Volume	Temperature	Acceptance Criterion
USP apparatus II (Paddle)	75 rpm	pH 6.8 buffer with 1.25% CTAB/ 1000 mL	37.0 ± 0.5 °C	Q= (b)(4)% in 45 minutes

Bridging: The Applicant has provided pharmacokinetic (PK) data to demonstrate bioequivalence (BE) between the LD, TASIGNA® (nilotinib) Capsules, 50 mg, 150 mg, and 200 mg EQ Base and the proposed drug product, Nilotinib Tablets, 71 mg, and 95 mg. The adequacy of the PK studies and bioequivalence between the LD and proposed product will be determined by the Office of Clinical Pharmacology (OCP), recommendation is pending assessment.

Formulation bridging: The commercial formulation is identical (Pg 19) to the clinical formulation.

Biowaiver: The Applicant has conducted clinical studies for both strengths. Biowaiver is neither requested nor needed.

Overall recommendation: From a Biopharmaceutics perspective, NDA 219293 for Nilotinib Tablets, 71 mg, and 95 mg is recommended for APPROVAL.

CQAs	Initial Risk Ranking	Comments	Updated Risk Ranking	Comments
(b) (4)		(b) (4)		(b) (4)
	Medium		Low	
	Medium		Low	

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
New NDA (Seq 0001)	6/21/2023
IR response (Seq 0015)	8/8/2024

Highlight Key Issues from Last Cycle and Their Resolution: Not Applicable

Concise Description of Outstanding Issues *(list bullet points with key information and update as needed)*: Not Applicable

B. 2. DISSOLUTION METHOD AND ACCEPTANCE CRITERIA

Assessment: Adequate

Based on the solubility data[1] (PDR, Pg 13) provided by the Applicant, (b) (4) nilotinib tartrate demonstrates pH-dependent solubility, with high solubility at pH 1.2 and pH 2.0, and low solubility at pH 3.0 and above.

(b) (4)

(b) (4)

Saturation solubility of nilotinib tartrate (37 °C)

Media pH	(b) (4) (mg/mL)
1.2	2.013±0.027
2.0	0.481±0.009
3.0	0.085±0.007
4.5	0.000±0.000
6.8	0.000±0.000

(b) (4)

The Applicant originally (PDR, Pg 61) proposed the following quality control dissolution method and acceptance criterion for the proposed drug product:

Apparatus	Speed	Medium	Volume/ Temperature	Acceptance Criterion
USP Apparatus II (Paddle)	75 rpm	pH 6.8 Phosphate buffer with 1.25% CTAB	1000 mL/ 37 ± 0.5 °C	Q= (b) (4) % in (b) (4) minutes

The Applicant submitted dissolution method development report[2] to justify the parameters and demonstrate the discriminating ability of the proposed dissolution method, and justification of selected testing parameters.

Dissolution medium selection: (b) (4)

(b) (4)

[1] \\CDSESUB1\EVSPROD\nda219293\0001\m3\32-body-data\32p-drug-prod\nilotinib-tablet\32p2-pharm-dev\pharmaceutical-development-dissolution-report.pdf
[2] \\CDSESUB1\EVSPROD\nda219293\0001\m3\32-body-data\32p-drug-prod\nilotinib-tablet\32p2-pharm-dev\pharmaceutical-development-dissolution-report.pdf

(b) (4)

Discriminating ability: The Applicant has identified various Critical Bioavailability Attributes (CBAs: (b) (4) , and tablet hardness) to evaluate the discriminating ability of the proposed dissolution method (1000 mL pH 6.8 with 1.25% CTAB, USP apparatus II, 75 rpm).

(b) (4)

(b) (4)

5) **Tablet hardness:** The dissolution profiles (Pg 49) for the drug product batches with lower ((b) (4) kP) and higher ((b) (4) kP) hardness were similar to the drug product batches with target hardness ((b) (4) kP).

The proposed dissolution method demonstrated sensitivity to the (b) (4) , and the Applicant has provided appropriate controls for (b) (4) in the drug product release and stability specifications.

Acceptance criterion: The Applicant initially proposed the acceptance criterion of "Q= (b) (4) % in (b) (4) minutes". However, based on the dissolution data[4] for pivotal batches, the proposed acceptance criterion is too wide and not acceptable. Therefore, a data-driven acceptance criterion of "Q= (b) (4) % in 45 minutes" was recommended in the IR[5] sent on 6/20/24. The Applicant accepted the recommendation to revise the acceptance criterion and provided updated drug product batch release and stability specifications in their response[6] submitted on 8/8/2024.

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 throughout stability program/shelf-life:

Final Approved Dissolution Method and Interim Acceptance Criterion:

Apparatus Type	Rotation Speed	Medium/ Volume	Temp	Acceptance Criterion
USP apparatus II (Paddle)	75 rpm	pH 6.8 buffer with 1.25% CTAB/ 1000 mL	37.0 ± 0.5 °C	Q= (b) (4) % in 45 minutes

[4] \\CDSESUB1\EVSPROD\nda219293\0001\m2\27-clin-sum\summary-biopharm-dissolution-profile-pivotal-qc-media.pdf
[5] \\CDSESUB1\EVSPROD\nda219293\0015\m1\us\annex-1-fda-ir-letter.pdf
[6] \\CDSESUB1\EVSPROD\nda219293\0015\m1\us\annex-3-response-to-ir-letter.pdf

B. 3. BRIDGING

Assessment: Adequate

Bridging to the listed drug: Applicant has provided PK data to demonstrate bioequivalence between the LD, TASIGNA® (nilotinib) Capsules, 50 mg, 150 mg, and 200 mg EQ Base and the proposed drug product, Nilotinib Tablets, 71 mg, and 95 mg. The adequacy of the PK studies and bioequivalence between the LD and proposed product will be determined by the Office of Clinical Pharmacology (OCP). The OCP's review of pharmacokinetic studies remains pending.

Manufacturing site: The drug product manufacturing site for clinical[7] batches and commercial[8] batches is the same (Catalent Pharma, Somerset, NJ).

Formulation bridging: The commercial formulation is identical[9] (Pg 19) to the clinical formulation.

B. 4. BIOWAIVER REQUEST

Assessment: Not Applicable

The Applicant has conducted[10] clinical studies for both strengths. Biowaiver is neither requested nor needed.

OVERALL CONCLUSION/RECOMMENDATION:
From a Biopharmaceutics perspective, NDA 219293 for Nilotinib Tablets, 71 mg, and 95 mg is recommended for APPROVAL.

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None.

[7] \\CDSESUB1\EVSPROD\nda219293\0001\m3\32-body-data\32p-drug-prod\nilotinib-tablet\32p5-contr-drug-prod\32p54-batch-analys\batch-analyses-nilotinibtablets71mg.pdf
[8] \\CDSESUB1\EVSPROD\nda219293\0007\m1\us\fda-form-356h-0007-signed.pdf
[9] \\CDSESUB1\EVSPROD\nda219293\0001\m2\25-clin-over\clinical-overview.pdf
[10] \\CDSESUB1\EVSPROD\nda219293\0001\m1\us\11215-bio-waiver.pdf

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