CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219122Orig1s000

PRODUCT QUALITY REVIEW(S)

Title:	NDA IQA Template Title Page- EXEC SUMMARY
Document ID:	OPQ-ALL-TEM-0040
Effective Date:	Revision: 00
Total Pages:	5

Template Revision: 03

Office of Pharmaceutical Quality

New Drug Application (NDA)
Integrated Quality Assessment Template

NDA Executive Summary

1. Application/Product Information

NDA Number	219122		
Applicant Name	Azurity Pharmaceuticals		
Drug Product Name	BRYNOVIN (sitagliptin) oral solution, 25 mg/mL		
Dosage Form	Solution		
Proposed Strength(s)	25 mg /mL		
NDA Classification	Type 5 – New Formulation or New Manufacturer		
Route of Administration	Oral		
Maximum Daily Dose	100 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	To improve glycemic control in adults with type 2 diabetes mellitus.		
Drug Product Description	Clear, colorless, to nearly colorless aqueous solution filled in a 125 mL Type (b) (4) glass (b) (4) with CR closure.		
Co-packaged product information	NA		
Device information	Not applicable		
Storage Temperature/ Conditions	Store at 2°C to 8°C in the original container		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Daniel Jansen	Zhengfu Wang
	Drug Product/ Labeling	Dan Berger	Muthukumar Ramaswamy
	Manufacturing	Naresh Pavurala	Erin Kim
	Biopharmaceutics	NA	NA

	Microbiology	Xia Xu	Nandini Bhattacharya
	Other (specify)	-	-
	RBPM	Oluwafunmike (Funke) Ajomale	
	ATL	Muthukumar Ramaswamy	
Consults			

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: 12 months from the date of manufacture, when stored at 2°C to 8°C in the original container.

b. Additional Comments for Action - none

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

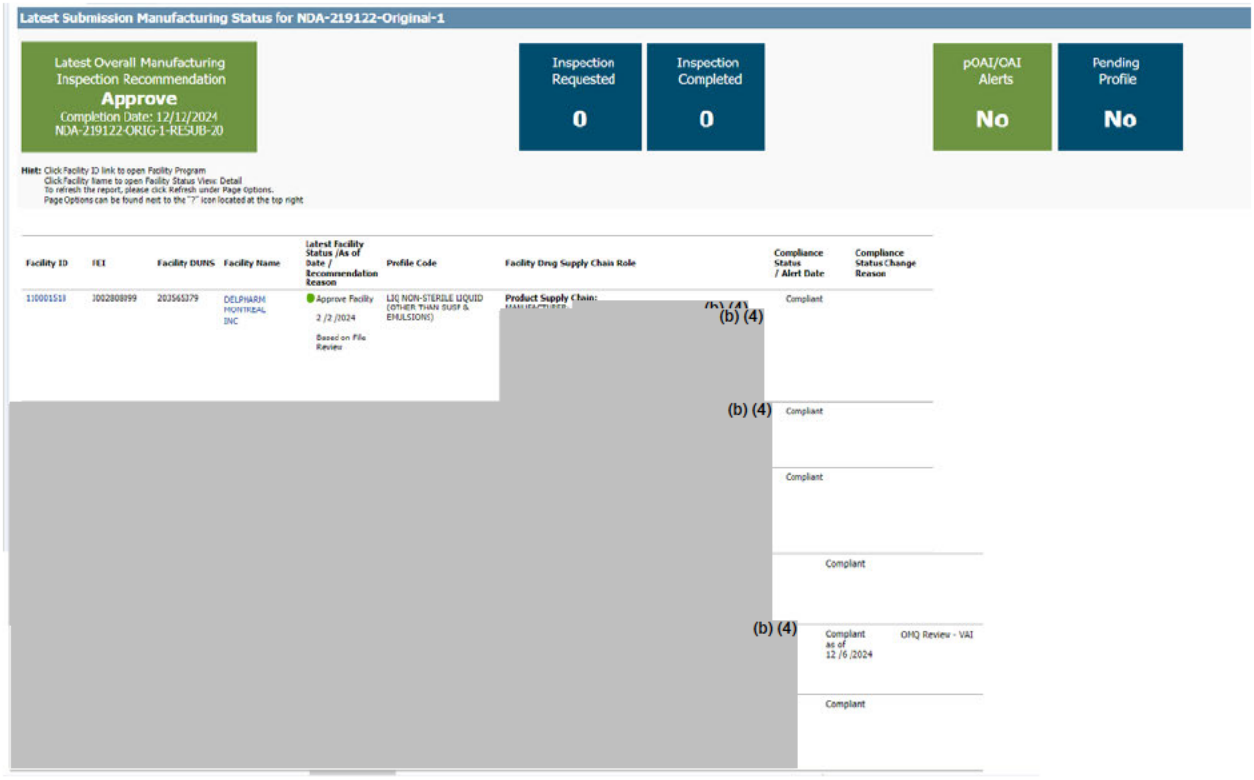
The Office of Pharmaceutical Quality Review team has assessed the Chemistry, Manufacturing, and Controls (CMC) information and determined that the new drug application (NDA) meet all applicable standards to support the approval of the drug product. As such, OPQ recommends approval of this NDA from a quality perspective.

The proposed product sitagliptin oral solution, 25 mg/mL is a clear, colorless to nearly colorless aqueous solution filled in a 125 mL amber glass bottle. The recommended storage condition for the drug product is 2°C to 8°C. The drug product is intended for administration using an oral dosing syringe.

NDA 219122 was originally submitted January 4, 2024. The OPQ did not recommend the approval of this application due to potential official action indicated alert (pOAI) for the drug substance manufacturing facility (b) (4) The compliance status of all the other manufacturing facilities associated with this application was acceptable. There were no deficiencies related to drug substance, drug product, manufacturing process, labeling, and microbiology sections of this application during first cycle review. A shelf-life of 12 months from the date of manufacture, was granted for the drug product, when stored at 2°C to 8°C in the original container. The proposed in-use period of 90 days for storage at 5°C, after first opening is acceptable. For additional details, refer to OPQ's Integrated Quality Assessment for NDA 219122 dated October 19, 2024, and September 25, 2024, in DARRTS.

The applicant resubmitted the application on November 18, 2024, with updated facility information in Form 356h and indicated that the drug substance manufacturer has provided responses to FDA inspection report on October 21, 2024.

The OPMA facility reviewer has reviewed the compliance status of this application. At this time, the compliance status of the drug substance manufacturing facility is voluntary action indicated (VAI). The status of all the facilities associated with this application are acceptable. As of 12/12/2024, the Overall Manufacturing Inspection recommendation for NDA 219122 is approve. For additional details, please refer to OPMA review dated 12/19/2024 in Panorama. Panorama screen shot of facility status is shown below.



The applicant also provided updated label information. There are no changes to the drug substance, drug product, manufacturing process or microbiological control information in the NDA.

Overall, OPQ recommends approval of this NDA from a quality 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	**-**	**Adequate**
Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**N/A**
Microbiology	**-**	**Adequate**

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:

Additional Lifecycle Comments:
None

Muthukumar Ramaswamy 12-19-2024

Application Technical Lead Name and Date:

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/s/

MUTHUKUMAR RAMASWAMY
12/19/2024 04:13:24 PM

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Dosage Form	Solution		
Proposed Strength(s)	25 mg /mL		
NDA Classification	Type 5 – New Formulation or New Manufacturer		
Route of Administration	Oral		
Maximum Daily Dose	100 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	To improve glycemic control in adults with type 2 diabetes mellitus.		
Drug Product Description	Clear, colorless, to nearly colorless aqueous solution filled in a 125 mL Type (b) (4) glass (b) (4) with CR closure.		
Co-packaged product information	NA		
Device information	Not applicable		
Storage Temperature/ Conditions	Store at 2°C to 8°C in the original container		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Daniel Jansen	Zhengfu Wang
	Drug Product/ Labeling	Dan Berger	Muthukumar Ramaswamy
	Manufacturing	Naresh Pavurala	Erin Kim
	Biopharmaceutics	NA	NA

	Microbiology	Xia Xu	Nandini Bhattacharya
	Other (specify)	-	-
	RBPM	Oluwafunmike (Funke) Ajomale	
	ATL	Muthukumar Ramaswamy	
Consults			

2. Final Overall Recommendation - Complete Response

Deficiencies:

Following a CGMP inspection of (b) (4) listed in this application, FDA conveyed deficiencies to the representative of the facility. Satisfactory responses from the facility are needed before this application can be approved. The facility's satisfactory responses are dependent on FDA's determination that the facility has come into compliance with CGMP and may require re-inspection of the facility. The deficiencies identified during the inspection may not be specific to your pending application; therefore, you should coordinate with the facility for timely resolution. Please refer to Compliance Program CP 7356.002 for guidance on post inspection activities. Following resolution of the CGMP inspection, FDA may need to conduct a PAI of the facility. Satisfactory outcomes of both the PAI and the CGMP inspections will be needed prior to an approval of the application.

As the applicant, we do not expect a response to this facility-related deficiency when responding to any other deficiencies cited in this or other information request or discipline review letters. Instead, please work with the facility, as applicable, in resolving the related deficiencies.

4. Basis for Recommendation:

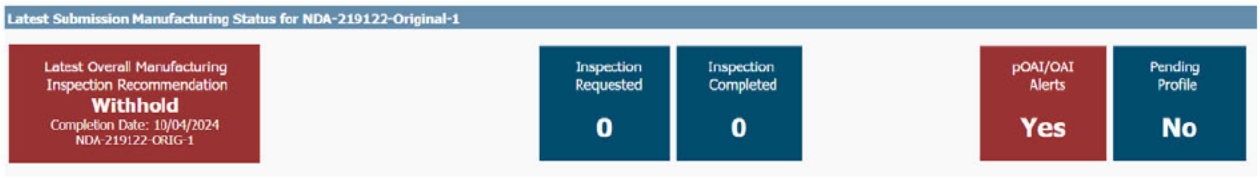
a. Summary of Rationale for Recommendation:
The Office of Pharmaceutical Quality Review team has assessed the Chemistry, Manufacturing, and Controls (CMC) information and determined that the new drug application (NDA) does not meet all applicable standards to support the approval of the drug product. As such, OPQ does not recommend approval of this NDA from a quality perspective.

The proposed product sitagliptin oral solution, 25 mg/mL is a clear,

colorless to nearly colorless aqueous solution filled in a 125 mL amber glass bottle. The recommended storage condition for the drug product is 2°C to 8°C. The drug product is intended for administration using an oral dosing syringe.

The OPQ's Integrated Quality Assessment for NDA 219122 dated September 25, 2024 in DARRTS indicated that all the facilities associated with this application are acceptable and the application was not recommended for approval due to inadequate control strategy to limit the levels of nitrosamine impurity, (b) (4) in the finished product below the FDA-established lifetime daily acceptable intake of (b) (4) ng/day. On (b) (4) As a result, the applicant's proposed control strategy to limit the (b) (4) levels in the drug product to NMT (b) (4) ppm during shelf-life will not be considered a deficiency. The proposed limit of NMT (b) (4) ppm for (b) (4) in the drug product meets the FDA-established daily acceptable intake of (b) (4) ng/day. Therefore, the drug product review team's recommendation is adequate. Based on stability data, the drug product reviewer granted a shelf-life of 12 months for the drug product, when stored at 2-8°C. For details, refer to CMC review for drug product in Panorama under NDA 219122.

Following a cGMP inspection of (b) (4) FDA conveyed deficiencies to the representative of the facility. As of 10/1/2024, the compliance status of (b) (4) is changed to withhold due to potential official action indicated alert (pOAI). Satisfactory responses from the facility are needed before this application can be approved. The facility's satisfactory responses are dependent on FDA's determination that the facility has come into compliance with CGMP and may require re-inspection of the facility. All the other manufacturing facilities associated with this application are acceptable at this time. Therefore, the OPMA facility assessment recommendation for NDA 219122 is inadequate. Panorama screen shot of latest overall manufacturing inspection recommendation is shown below. For details, refer to OPMA review for process, and facilities in Panorama under NDA 219122.



Therefore, the OPQ review team does not recommend approval of this NDA from a quality 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	**-**	**Adequate**
Manufacturing	**-**	**Inadequate**
Biopharmaceutics	**-**	**N/A**
Microbiology	**-**	**Adequate**

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:

Additional Lifecycle Comments:
None

Muthukumar Ramaswamy 10-09-2024

Application Technical Lead Name and Date:

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/s/

MUTHUKUMAR RAMASWAMY
10/10/2024 11:36:40 AM
This CMC review is an update to previously filed OPQ IQA for NDA 219122 in DARRTS on Sep 25, 2024

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Proposed Strength(s)	25 mg /mL		
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Route of Administration	Oral		
Maximum Daily Dose	100 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	To improve glycemic control in adults with type 2 diabetes mellitus.		
Drug Product Description	Clear, colorless, to nearly colorless aqueous solution filled in a 125 mL Type (b) (4) glass (b) (4) with CR closure.		
Co-packaged product information	NA		
Device information	Not applicable		
Storage Temperature/ Conditions	Store at 2°C to 8°C in the original container		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Daniel Jansen	Zhengfu Wang
	Drug Product/ Labeling	Dan Berger	Muthukumar Ramaswamy
	Manufacturing	Naresh Pavurala	Erin Kim
	Biopharmaceutics	NA	NA

	Microbiology	Xia Xu	Nandini Bhattacharya
	Other (specify)	-	-
	RBPM	Oluwafunmike (Funke) Ajomale	
	ATL	Muthukumar Ramaswamy	
Consults			

2. Final Overall Recommendation - Complete Response

Deficiencies: Your resubmission contains inadequate control strategy to limit the levels of nitrosamine impurity, (b) (4) in the finished product below the FDA-established lifetime daily acceptable intake of (b) (4) ng/day during shelf-life.

Specifically, we note that:

a) Your proposed stability acceptance limit of (b) (4) ppm for nitrosamine impurity, (b) (4) in the drug product exceeds the (b) (4) ppm limit and thereby, does not meet the established lifetime daily acceptable intake level of (b) (4) ng/day, when dosed at 100 mg/day (MDD).
b) (b) (4) levels in aged drug product batches exceed (b) (4) ppm and the data submitted in the NDA indicate that the product does not meet the established lifetime daily acceptable intake of (b) (4) ng/day during shelf-life.
c) Inadequate batch release and stability data to support that (b) (4) levels in the drug product will be controlled below (b) (4) ppm through shelf-life.

To resolve these deficiencies, in your resubmission, provide batch release and stability data including in-use stability data at the end of shelf-life from 3 commercial scale batches manufactured at Delpharm to support the control of nitrosamine impurity, (b) (4) in the finished product below the FDA established lifetime daily acceptable intake of (b) (4) ng/day at release and during shelf-life.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

The Office of Pharmaceutical Quality Review team has assessed the Chemistry, Manufacturing, and Controls (CMC) information and determined that the new drug application (NDA) does not meet all applicable standards to support the approval of the drug product. As such, OPQ does not recommend approval of this NDA from a quality perspective.

The proposed product sitagliptin oral solution, 25 mg/mL is a clear, colorless to nearly colorless aqueous solution filled in a 125 mL amber glass bottle. The recommended storage condition for the drug product is 2°C to 8°C. The drug product is intended for administration using an oral dosing syringe.

Except for (b) (4) impurity control in the drug product, there are no deficiencies related to drug substance, drug product, manufacturing process, facility, labeling, and microbiology sections of this application. All facilities associated with this NDA are adequate. For additional details, refer to CMC reviews for drug substance, drug product, microbiology, labeling, process, and facilities in Panorama under NDA 219122.

The drug product review team does not recommend the approval of the application due to deficiencies related to control of the nitrosamine impurity, (b) (4) in the drug product below (b) (4) ppm. Based on available manufacturing control information, the applicant has proposed to control the (b) (4) levels in drug substance at NMT (b) (4) ppm and in the drug product at NMT (b) (4) ppm during release and at NMT (b) (4) ppm during shelf-life.

The applicant's proposed shelf-life limit of (b) (4) ppm for (b) (4) does not meet the established lifetime daily acceptable intake level of (b) (4) ng/day, when dosed at a maximum daily dose of 100 mg/day.

Available stability data from commercial manufacturing facility does not support that the batches would meet the (b) (4) limit of (b) (4) ppm after 6 months of storage at 2°C to 8°C. Late in the review cycle, the applicant proposed additional manufacturing controls (b) (4) (b) (4) but did not provide any release and stability data for drug product from commercial scale batches to support that these batches would meet (b) (4) ppm limit during shelf-life. At this time, manufacturing control information provided in the NDA for the control of (b) (4) in the drug product is inadequate. Therefore, the OPQ review team does not recommend approval of this NDA from a quality perspective.

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

Recommendation by Subdiscipline:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Inadequate**
Quality Labeling	**-**	**Adequate**

Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**N/A**
Microbiology	**-**	**Adequate**

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:

Additional Lifecycle Comments:
None

Muthukumar Ramaswamy 09-25-2024

Application Technical Lead Name and Date:

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CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:

The proprietary name was edited to remove "HCl" in applicable sections, and replacement of [redacted] (b) (4) in section 11 with "sweetener/flavoring agent". With these edits, the prescribing information meets all regulatory requirements from a CMC perspective.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	TRADENAME	Adequate
Established name(s)	Sitagliptin ~~Hydrochloride~~	Adequate, following removal of hydrochloride
Route(s) of administration	Oral	Adequate
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	25 mg/mL oral solution	Adequate.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	NA	NA
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.	NA	NA

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Information Provided in the NDA	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)	NA	NA

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Oral solution.	Adequate
Strength(s) in metric system	25 mg/mL	Adequate
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance	The salt policy is applied for the DP strength.	Adequate
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting	Oral solution 25 mg/mL as a clear, colorless to nearly colorless aqueous solution in an amber glass bottle.	Adequate
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	NA	NA
For injectable drug products for parental administration, use appropriate labeling term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	NA	NA

1.2.3 Section 11 (DESCRIPTION)

Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	TRADENAME, sitagliptin	Adequate
Dosage form(s) and route(s) of administration	Oral solution	Adequate
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	Each mL contains 27.24 mg of sitagliptin HCl, equivalent to 25 mg of sitagliptin.	Adequate
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	Butylated hydroxyanisole, citric acid anhydrous, edetate disodium, hydroxyethyl cellulose, methylparaben sodium, polysorbate 80, purified water and sodium citrate dihydrate, sweetener/flavoring agent.	Adequate following edits to replace (b) (4)
For parenteral injectable dosage forms, include name and quantities of all inactive ingredients.	NA	NA
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	NA	NA
Statement of being sterile (if applicable)	NA	NA
Pharmacological/ Therapeutic class	DPP-4 enzyme inhibitor	Adequate
Chemical name, structural formula, molecular weight	Chemical name*, 461.79 g/mol, $C_{16}H_{15}F_6N_5O \cdot HCl.H_2O$	Adequate
If radioactive, statement of important nuclear characteristics.	NA	NA
Other important chemical or physical properties (such as pKa or pH)	White to off-white powder soluble in water.	Adequate

*7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine HCl monohydrate.

Section 11 (DESCRIPTION) Continued

Item	Information Provided in the NDA	Assessor's Comments
For oral prescription drug products, include gluten statement if applicable	NA	NA
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"	NA	NA

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Oral solution	Adequate
Strength(s) in metric system	25 mg/mL	Adequate
Available units (e.g., bottles of 100 tablets)	Each bottle contains 120 mL oral solution.	Adequate with edits
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	Clear colorless, to nearly colorless aqueous solution, NDC 24338-017-01	Adequate
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	NA	NA
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.	NA	NA

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

Item	Information Provided in the NDA	Assessor's Comments
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.)	Protect from light. Avoid excessive heat and freezing. Discard unused portion 90 days after first opening.	Adequate
If the product contains a desiccant, ensure the size and shape differ from the dosage form and desiccant has a warning such as "Do not eat."	NA	NA
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Store refrigerated at 2°C to 8°C (36°F to 46°F) [see USP];	Adequate
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: "Not made with natural rubber latex. Avoid statements such as "latex-free."	NA	NA
Include information about child-resistant packaging	Present	Adequate

1.2.5 Other Sections of Labeling

No other sections of the labeling contain product quality information.

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Information Provided in the NDA	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	Manufactured for: Azurity Pharmaceuticals, Inc. Woburn, MA 01801	Adequate

2.0 PATIENT LABELING

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

Storage conditions and the inactive ingredient list is provided in the Medication Guide. Edits have been made to remove a trade name from the inactive ingredients and to remove "HCl" from the proprietary name. The drug product strength in mg/mL was added to the title. Following the changes made, this information complies with all regulatory requirements from a CMC perspective.

3.0 CARTON AND CONTAINER LABELING

3.1 Container Label

(b) (4)

3.2 Carton Labeling

1 Page(s) of Draft Labeling has been Withheld in Full as b4 (CCI/TS) immediately following this page

Item	Information Provided in the NDA	Assessor's Comments about Bottle and carton Labeling
Proprietary name, established name, and dosage form (font size and prominence	Brynovin (sitagliptin ~~HCl~~) oral solution	Adequate, addressed based on comment provided in the PI.
Dosage strength	25 mg/mL	Adequate
Route of administration	oral solution	Adequate
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	Each 1 mL dose contains 27.24 mg of sitagliptin hydrochloride, equivalent to 25 mg sitagliptin.	Adequate
Net contents (e.g. tablet count)	120 mL	Adequate
"Rx only" displayed on the principal display	Present	Adequate
NDC number	24338-017-01	Adequate
Lot number and expiration date	Present on bottle only.	Adequate, addressed by DMEPA.
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	Store at 2°C to 8°C (b) (4) to 46°F)	Adequate
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	NA	NA
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.	NA	NA
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	NA	NA
Bar code	Present	Adequate

Item	Information Provided in the NDA	Assessor's Comments about Bottle Labeling
Name of manufacturer/distributor	Manufactured for: Azurity Pharmaceuticals, Inc. Woburn, MA 01801, USA	Adequate
Medication Guide (if applicable)	Storage conditions and active/inactive ingredients listed.	Adequate following edits made.
No text on Ferrule and Cap overseal	NA	NA
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.	NA	NA
And others, if space is available	NA	NA

Assessment of Carton and Container Labeling: ***Adequate***
Address removal of HCl. With the required edits, the labels comply with all regulatory requirements from a CMC perspective.

ITEMS FOR ADDITIONAL ASSESSMENT

None

Overall Assessment and Recommendation:

Edits to the carton and container labels have been addressed by OPQ and DMEPA recommendations. Following edits made, the Prescribing Information, Medication Guide and labels comply with all regulatory requirements from a CMC perspective.

Primary Labeling Assessor Name and Date:

Dan Berger September 17, 2024

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

Muthukumar Ramaswamy September 17, 2024

Dan Berger

Digitally signed by Dan Berger
Date: 9/17/2024 03:14:12PM
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Muthukumar Ramaswamy

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CHAPTER VII: MICROBIOLOGY

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

Product Information	Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
NDA Number	219122
Assessment Cycle Number	01
Drug Product Name/ Strength	BRYNOVIN (Sitagliptin Hydrochloride Oral Solution), 25 mg/mL
Route of Administration	Oral
Applicant Name	Azurity Pharmaceuticals, Inc.
Therapeutic Classification/ OND Division	Division of Diabetes, Lipid Disorders and Obesity
Manufacturing Site	Delpharm Montreal, Inc. 3535 aut Transcanadienne Pointe-Claire, QC, H9R 1B4, Canada FEI # 3002808099 DUNS # 203565379
Method of Sterilization	Drug product is non sterile.

Assessment Recommendation: **Adequate**

Assessment Summary: This is a multi-dose non-sterile oral drug product. The manufacturing process is to be controlled for microbial quality and absence of specified microorganisms. Supporting data meet the quality microbiology review criteria.

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
Supporting document # 1 (Seq-0001)	01/04/2024
Supporting document # 5 (Seq-0005)	03/26/2024
Supporting document # 11 (Seq-0011)	05/20/2024

Highlight Key Issues from Last Cycle and Their Resolution: None.

Remarks: N/A

Concise Description of Outstanding Issues: None.

Supporting Documents: None.

S DRUG SUBSTANCE

The drug substance (Sitagliptin Hydrochloride), manufactured by [redacted] (Karnataka, India), is supplied as [redacted]

Assessment: Drug substance is non-sterile. No quality microbiological testing is proposed.

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

Description of drug product

Sitagliptin Hydrochloride Oral Solution 25 mg/mL is a non-sterile, [redacted] aqueous solution packaged in a multi-dose amber glass bottle for oral administration.

Drug product composition

Ingredient	Function	mg/mL	% w/v
Sitagliptin Hydrochloride	Active	27.24*	0.27
Butylated Hydroxyanisole, NF	[redacted]		
Edetate Disodium, USP			
Sodium Citrate Dihydrate, USP			
Methylparaben Sodium, NF			
Citric Acid Anhydrous, USP			
Polysorbate 80, NF [redacted]			
[redacted]	Sweetener/ Flavoring Agent		
Hydroxyethyl Cellulose, NF [redacted]			
Purified Water, USP			

* 27.24 mg/mL of Sitagliptin Hydrochloride equivalent to 25 mg/mL of Sitagliptin Base.
QS = Quantity Sufficient

Description of container closure system

Components	Description	Manufacturer
Bottle	125 mL Amber Glass [redacted] Bottle	[redacted]
Closure	[redacted] Cap, [redacted] with liner	

Assessment: ***{Adequate}***

The drug product composition and container-closure system are adequately described. The container-closure system is adequate for the drug product oral administration.

P.2 PHARMACEUTICAL DEVELOPMENT

P.2.5 MICROBIOLOGICAL ATTRIBUTES

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/s/

MUTHUKUMAR RAMASWAMY
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