CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218710Orig1s000

PRODUCT QUALITY REVIEW(S)

Title:	NDA IQA Template Title Page-EXEC SUMMARY
Document ID:	OPQ-ALL-TEM-0040
Effective Date:	26 Sep 2023 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	NDA 218710
Applicant Name	Phathom Pharmaceuticals, Inc.
Drug Product Name	Voquezna (vonoprazan) Tablets, 10 mg
Dosage Form	Tablet
Proposed Strength(s)	10 mg
NDA Classification	Type 9 – New Indication Submitted as Distinct NDA – Consolidated
Route of Administration	Oral
Maximum Daily Dose	10 mg for the indication in this application and 20 mg for other indications approved in NDA 215151
Rx/OTC Dispensed	Rx
Proposed Indication	Treatment of heartburn associated with symptomatic non-erosive gastroesophageal reflux disease
Drug Product Description	Pharmaceuticals, Inc. has submitted this 505 (b)(1) application for Voquezna® (vonoprazan) Tablets, 10 mg indicated for the Treatment of heartburn associated with symptomatic non-erosive gastroesophageal reflux disease. The drug product in this application, Voquezna® Tablets, 10 mg was previously reviewed and approved for a different indication under NDA 215151 on November 1, 2023. This application was submitted as a distinct NDA for a new indication for the previously approved drug product. 10 mg tablets are pale yellow, oval, film-coated tablets debossed with “V10” on one side and plain on the other side. Each Voquezna tablet contains 10 mg of vonoprazan provided as 13.36 mg of vonoprazan fumarate as the active ingredient.

	Voquezna® 10 mg tablets also contain the following inactive ingredients: ascorbic acid, croscarmellose sodium, ferric oxide yellow, fumaric acid, hydroxypropyl cellulose, hypromellose, magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol 8000, and titanium dioxide. The inactive ingredients used in the tablet composition are all compendial materials. Voquezna® tablets are packaged as 30 tablets in high density polyethylene (HDPE) bottles with (b) (4) (b) (4) closures. Tablets should be stored at 20°C to 25°C (68°F to 77°F) and excursions permitted to 15°C to 30°C (59°F to 86°F).		
Co-packaged product information	N/A		
Device information	N/A		
Storage Temperature/ Conditions	20°C and 25°C (68°F and 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Friedrich Burnett, Ph.D.	Lawrence Perez, Ph.D.
	Drug Product/ Labeling	Hitesh, Shroff, Ph.D.	Hamid Shafiei, Ph.D. Julia Pinto, Ph.D.
	Manufacturing	Lloyd Alfonso, Ph.D.	Jean Tang, Ph.D.
	Biopharmaceutics	Tapash Ghosh, Ph.D.	Tapash Ghosh, Ph.D.
	Microbiology	N/A	N/A
	Other (specify) Environmental Assessment	Hitesh Shroff, Ph.D.	Hamid Shafiei, Ph.D.
	RBPM	Megan Nguyen	
	ATL	Hamid Shafiei, Ph.D.	

Consults	N/A

2. Final Overall Recommendation - Approval

The drug product in this application, Voquezna (vonoprazan) tablets, 10 mg was previously reviewed and approved on November 1, 2023, under NDA 215151 for a different indication. This application has been submitted as a distinct NDA for a new indication for Voquezna 10 mg tablets.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

- The applicant of this 505(b)(1) new drug application has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug substance, vonoprazan fumarate and the drug product, Voquezna (vonoprazan) Tablets, 10mg.
- The Office Pharmaceutical Manufacturing Assessment has made the overall recommendation of adequate for the facilities involved in this application.
- The CMC issues on labels/labeling have been satisfactorily addressed.
- The applicant's request for the categorical exclusion from the preparation of the environmental assessment has been granted.

Therefore, from the OPQ perspective, this NDA is recommended for **approval** with the expiration dating period of **24 months**.

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): Yes

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No

Comments:
None

Comparability Protocols (PACMP): No
Comments:
None

Additional Lifecycle Comments:
None

Application Technical Lead Name:

Hamid Shafiei, Ph.D.
Senior Pharmaceutical Quality Assessor
DPQA VII/OPQA II/OPQ

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CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information: Submitted on Sep 20, 2023 SDN 0001

(b) (4)

Item	Items 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		
Established name(s)[1]	Adequate	
Route(s) of administration	Adequate	
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored".	N/A	
For injectable drug products for 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).	Adequate	The following equivalency statement is in Sec. 11 DESCRIPTION: Each film-coated tablet contains 10 mg of vonoprazan, equivalent to 13.36 mg of vonoprazan fumarate.

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

1.1 FULL PRESCRIBING INFORMATION

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

3 DOSAGE FORMS AND STRENGTHS

(b) (4)

[redacted]

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	
Strength(s) in metric system	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (Tablets: 10 mg of drug-x hydrochloride).	Adequate The USP Salt Policy is adhered to. The tablet strength is based on the active moiety, vonoprazan.	The following equivalency statement is in Sec. 11 DESCRIPTION: Each film-coated tablet contains 10 mg of vonoprazan, equivalent to 13.36 mg of vonoprazan fumarate.
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for 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	

1.2.2 Section 3 (Section 11 DESCRIPTION)

(b) (4)

QUALITY ASSESSMENT

Item	Items 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)	Adequate	
Dosage form(s) and route(s) of administration	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)"	Adequate The USP Salt Policy is adhered to. The tablet strength is based on the active moiety, etrasimod	The following equivalency statement is in Sec. 11 DESCRIPTION: Each film-coated tablet contains 10 mg of vonoprazan, equivalent to 13.36 mg of vonoprazan fumarate.
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	Adequate	
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	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	
Chemical name, structural formula, molecular weight	Adequate	
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Adequate	

Section 11 (DESCRIPTION) Continued

Item	Items 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 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)

(b) (4)

Item	Items 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)	Adequate	
Strength(s) in metric system	Adequate	
Available units (e.g., bottles of 100 tablets)	Adequate	
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	

For injectable drug products for 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	

Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	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."*	N/A	
Include information about child-resistant packaging (if manufacturer choose to include)	Adequate	

1.2.6 Manufacturing Information After Section 17 (for drug products)

(b) (4)

Item	Items 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)
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	

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Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[2], (font size and prominence)	Adequate	
Strength(s) in metric system	Adequate	
Route(s) of administration	N/A	
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	Adequate	The following equivalency statement is present in bottle and carton labels. Each tablet contains: Vonoprazan.....10 mg (equivalent to 13.36 mg of Vonoprazan Fumarate).
Net contents (e.g., tablet count, volume of liquid)	Adequate	
"Rx only" displayed on the principal display	Adequate	
NDC	Adequate	
Lot number and expiration date	Adequate	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Adequate	
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	Not required on physicians' samples
Name of manufacturer/distributor /packer	Adequate	
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 relevant compendium, its difference shall be plainly stated on its label.	N/A	
And others if space is available.	Adequate	Do not accept if seal over bottle is broken or missing.

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

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[1]	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 differs from the dosage form.	N/A	
Active ingredient(s) (if applicable)	Adequate	
Alphabetical listing of inactive ingredients (if applicable)	Adequate	
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer	Adequate	

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

Assessment of PI: ***ADEQUATE***

Assessment of Carton and Container Labeling: ***ADEQUATE***

Assessment of Medication Guide: ***ADEQUATE***

ITEMS FOR ADDITIONAL ASSESSMENT: *None*

Overall Assessment and Recommendation:

The PI and container/carton labels are satisfactory from the CMC perspective.

The following comment should be conveyed to the NDA applicant.

- Please add the following statement to all container and carton labels:
  For oral use

This NDA is recommended for "**Approval**" from the labeling perspective.

Primary Labeling Assessor Name and Date:
Hitesh Shroff
OPQ, ONDP, DNDP II, Branch 4
XX-XX-2024

QUALITY ASSESSMENT

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

Julia Pinto, Ph.D.
Supervisory Chemist
OPQ, ONDP, DNDP II, Branch 3

Julia Pinto

Digitally signed by Julia Pinto
Date: 3/14/2024 01:51:28PM
GUID: 5050dbcb00001294a888a4bdc20a3a58

Hitesh Shroff

Digitally signed by Hitesh Shroff
Date: 3/14/2024 11:30:30AM
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Comments: The labeling is adequate from the CMC perspective.

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QUALITY REVIEW

BIOPHARMACUTICS
NDA: NDA 218710
Drug Product Name / Strength: Vonoprazan tablets, 10 mg
Route of Administration: Oral
Applicant Name: Phathom Pharmaceuticals, Inc.
Indication: Healing of all grades of **non-erosive** esophagitis and relief of heartburn
Submission date: 09/20/2023
Primary Reviewer: Tapash Ghosh, Ph.D.
Recommendation: Adequate

BACKGROUND:

The Applicant is seeking approval under 505(b)(1) regulatory pathways for Vonoprazan tablets, 10 mg, for oral administration, indicated for the healing of all grades of non-erosive esophagitis and relief of heartburn, and maintenance of healing of all grades of erosive esophagitis and relief of heartburn (NDA-218710-ORIG-1).

The 10 mg tablets in this application have been previously reviewed and approved under NDA 215151 and this application has been submitted only for adding a new indication (i.e., **non-erosive**) to the currently approved dug product. As this NDA 218710 was submitted prior to the approval of NDA 215151, a new NDA number has been assigned to this NDA; otherwise it would have come as an efficacy-supplement.

REVIEW SUMMARY:

In the original Biopharmaceutics review of NDA 215151 (https://panorama.fda.gov/task/view?ID=62e1652a0063f855ca0dc7a6533fa4bd), the following dissolution method and acceptance criterion was found acceptable fr the 10 mg tablet. As there is no change in the drug product, no further biopharmacetics review is needed for this NDA 218710.

1) Dissolution Method and Acceptance Criteria: Acceptable

The approved dissolution method and acceptance criterion for quality control and stability testing of the proposed Vonoprazan tablets, 10 mg, and 20 mg:

Apparatus	Rotation Speed (rpm)	Medium	Volume (mL)	Temperature	Acceptance Criterion
USP Apparatus 2 (Paddle)	50	Acetate buffer, pH 4.5	900	37±0.5°C	(b) (4)% in 15 minutes

CONCLUSION AND RECOMMENDATION:

Form a Biopharmaceutics perspective, NDA 218710Voquenza (vonoprazan) tablets, 10 mg is **adequate** for approval for the healing of all grades of non-erosive esophagitis and relief of heartburn, and maintenance of healing of all grades of erosive esophagitis and relief of heartburn.

Tapash Ghosh

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Date: 2/27/2024 11:41:31AM
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/s/

HAMID R SHAFIEI
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