



NDA 215152/S-003
NDA 215153/S-003

**SUPPLEMENT APPROVAL
PMR FULFILLED**

Phathom Pharmaceuticals, Inc.
Attention: Nancianne Knipfer, PhD, RAC
Vice President, Regulatory Affairs and Medical Writing
2150 East Lake Cook Road, Suite 800
Buffalo Grove, IL 60089

Dear Dr. Knipfer:

Please refer to your supplemental new drug application (sNDA) dated and received April 26, 2023, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

- NDA 215152: Voquezna Triple Pak (vonoprazan tablets; amoxicillin capsules; clarithromycin tablets) 20 mg, 500 mg, 500 mg, co-packaged
NDA 215153: Voquezna Dual Pak (vonoprazan tablets; amoxicillin capsules) 20 mg, 500 mg, co-packaged

This Prior Approval sNDA provides for changes to the prescribing information (PI) of Voquezna Triple Pak and Voquezna Dual Pak. The following changes were made to align with the PI for NDA 215151 for Voquezna (vonoprazan) tablets:

1. Revision of the **DOSAGE AND ADMINISTRATION (2)** section, **Recommended Dosage in Patients with Renal Impairment (2.3)** subsection and **Recommended Dosage in Patients with Hepatic Impairment (2.4)** subsection to replace the term (b) (4) with "Use is not recommended" in Tables 1 and 2.
2. Addition of Acute Tubulointerstitial Nephritis to the **WARNINGS and PRECAUTIONS (5)** section **Warnings and Precautions for VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK (5.1)** subsection with corresponding updates to the **PATIENT COUNSELING INFORMATION (17)** section.
3. Revision of the **ADVERSE REACTIONS (6)** section, **Clinical Trials Experience (6.1)** subsection, Other Adverse Reactions subheading, and **Postmarketing Experience with Components of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK (6.2)** subsection.
4. Addition of Interaction with Secretin Stimulation Test under the **DRUG INTERACTIONS (7)** section.
5. Revision of the **SPECIAL POPULATIONS (8)** section, **Renal Impairment (8.6)** subsection and **Hepatic Impairment (8.7)** subsection to replace the term (b) (4) with "Use of is not recommended."

6. Revision of the United States Adopted Name (USAN) name for vonoprazan fumarate under the **DESCRIPTION (11)** section.

In addition, the following sections were revised:

7. The **CLINICAL PHARMACOLOGY (12)** section, **Pharmacokinetics (12.3)** subsection Metabolism subheading, was updated based on the study results from Study TKD-BCS-10698 titled "Assessment of Relative Contribution of Phase 1 and Phase 2 Metabolic Enzymes to TAK-438 Metabolism and Cytochrome P450/Sulfotransferases Phenotyping."
8. Formatting changes were also made to the **DOSAGE AND ADMINISTRATION (2)** section.
9. Minor editorial changes were made throughout the PI.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling, with the following editorial revisions:

For the Recent Major Changes listed in the Highlights section, vertical lines are added to the left side of the **DOSAGE AND ADMINISTRATION (2)** section, **Recommended Dosage in Patients with Hepatic Impairment (2.4)** subsection, and **WARNINGS and PRECAUTIONS (5)** section **Warnings and Precautions for VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK (5.1)** subsection Interactions with Diagnostic Investigations for Neuroendocrine Tumors subheading to mark the corresponding new or modified text in the full prescribing information (FPI).

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study(ies) requirement for these applications because necessary studies are impossible or highly impracticable as the prevalence of *H. pylori* infection that requires treatment is low in the pediatric population.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated March 31, 2023 containing the final report for the following postmarketing requirement listed in the May 2, 2022 approval letter.

4270-4 Conduct a post-marketing in vitro reaction phenotyping study with selective chemical inhibitors to determine the role of cytochrome P450 (CYP) enzymes (e.g., CYP3A4/5, CYP2B6, CYP2C19, CYP2C9, and CYP2D6) in vonoprazan metabolism at clinically relevant concentrations under the linear condition. This study should be designed and conducted in accordance with the FDA Guidance for Industry entitled “In Vitro Drug Interaction Studies – Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions”. Depending on the results of this in vitro study, additional studies may be needed.

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there are postmarketing requirements listed in the May 2, 2022 approval letter that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Eva Zuffova, PhD, Senior Regulatory Project Manager, at (301) 796-0697.

Sincerely,

{See appended electronic signature page}

Dmitri Iarikov, MD, PhD
Deputy Director
Division of Anti-Infectives
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE:

- Content of Labeling
 - Prescribing Information

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DMITRI IARIKOV
07/31/2024 05:25:11 PM