CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215151Orig1s000

OTHER ACTION LETTERS

NDA 215151

COMPLETE RESPONSE

Phathom Pharmaceuticals, Inc.
Attention: Esha Desai, MS, RAC
Director, Regulatory Affairs
2150 East Lake Cook Road, Suite 800
Buffalo Grove, IL 60089

Dear Ms. Desai:

Please refer to your new drug application (NDA) dated and received March 11, 2022, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Voquezna (vonoprazan) tablets.

We also acknowledge receipt of your amendment, dated January 23, 2023 in response to our advice letter dated December 23, 2022, which was not reviewed for this action. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance or the drug product are inadequate to preserve its identity, strength, quality, purity, stability, and bioavailability (21 CFR 314.125(b)(1)).

A type B meeting was held on September 6, 2022 under NDAs 215152/215153 to discuss the finding of (b) (4) a (b) (4) impurity, in the vonoprazan fumarate drug substance and vonoprazan tablets. (b) (4)

(b) (4)

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To address these deficiencies:

1. Revise the acceptance criterion [redacted] (b) (4) for the drug product release and stability specifications.

2. Perform a root cause investigation [redacted] (b) (4)

3. Submit long term, intermediate (if applicable), and accelerated stability data for at least three batches for each strength (i.e., 10 mg and 20 mg tablets) representative of the to-be-marketed product demonstrating that the stability data meet the updated specifications, including acceptance criterion [redacted] (b) (4). Refer to the guidance for industry, *Q1A(R2) Stability Testing of New Drug Substances and Products* (November 2003).

We encourage you to request a meeting to discuss your plans to address these deficiencies prior to resubmission.

PRESCRIBING INFORMATION

Submit draft labeling that is responsive to our communication dated January 12, 2023.

Prior to resubmitting the labeling, use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances. In addition, submit updated content of labeling [21 CFR 314.50(l)(1)(i) in structured product labeling (SPL) format as described at FDA.gov.[2]

To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Word version. The marked-up copy should include annotations that support any proposed changes.

Your proposed Prescribing Information (PI) must conform to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57. As you develop your proposed PI, we encourage you to review the labeling review resources on the Prescription Drug Labeling Resources[3] and Pregnancy and Lactation Labeling Final Rule[4] websites, which include:

[2] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

[3] https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources
[4] https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information in the PI on pregnancy, lactation, and females and males of reproductive potential
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading
- Additional resources for the PI, patient labeling, and carton/container labeling

CARTON AND CONTAINER LABELING

Submit draft carton and container labeling based on our proposed revisions dated November 22, 2022.

PROPRIETARY NAME

Please refer to our correspondence dated, April 28, 2022, which addresses the proposed proprietary name, Voquezna. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

(1) Describe in detail any significant changes or findings in the safety profile.

(2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.

- Present tabulations of the new safety data combined with the original application data.

- Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.

- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

(3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

(4) Provide case report forms and narrative summaries for each subject who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.

(5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.

(6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

(7) Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

(8) Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial

response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Maureen Dewey, Senior Regulatory Project Manager, at (301) 796-0845.

Sincerely,

{See appended electronic signature page}

Juli Tomaino, MD, MS
Deputy Division Director
Division of Gastroenterology
Office of Immunology and Inflammation
Center for Drug Evaluation and Research

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/

JULI A TOMAINO
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