



NDA 050824/S-010

SUPPLEMENT APPROVAL

Cumberland Pharmaceuticals, Inc.
Attention: Beth A. Zaborny
Director, Regulatory Affairs
2525 West End Avenue, Suite 950
Nashville, TN 37203

Dear Ms. Zaborny:

Please refer to your supplemental new drug application (sNDA) dated and received December 13, 2021, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Omeclamox-Pak (omeprazole delayed-release capsules, clarithromycin tablets and amoxicillin capsules, 20 mg/500 mg/500 mg).

We also refer to our letter dated November 22, 2021, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for proton pump inhibitors (PPI). This information pertains to the risk of Severe Cutaneous Adverse Reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP).

This changes being effected sNDA provides for revisions to the Prescribing Information (PI) for Omeclamox-Pak, consistent with our November 22, 2021, letter.

Specifically, the **WARNINGS AND PRECAUTIONS (5)** section, has been revised to include **Severe Cutaneous Adverse Reactions (5.2)** subsection to state that SCARs, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported with the components of OMECLAMOX-PAK: omeprazole, clarithromycin, and amoxicillin.

Additional revisions are also included in the following sections and subsections of the attached (PI): **HIGHLIGHTS OF PRESCRIBING INFORMATION, ADVERSE REACTIONS (6)** section, **Post-Marketing Experience with the Individual Components of OMECLAMOX-PAK (6.3)** subsection, under the Omeprazole subheading, and the **PATIENT COUNSELING INFORMATION (17)** section.

Other requested changes not required under section 505(o)(4) of the FDCA have been made to the labeling to include SCARs: SJS, TEN, DRESS and AGEP for the **Clarithromycin** and **Amoxicillin** components of Omeclamox-Pak in the **WARNINGS AND PRECAUTIONS, (5)** section, **Severe Cutaneous Adverse Reactions (5.2)**

subsection and in the **ADVERSE REACTIONS (6)** section, **Postmarketing Experience with the Individual Components of Omeclamox-Pak (6.3)** subsection, under the *Skin* subheading under the Clarithromycin and Amoxicillin subheadings.

Furthermore, the **ADVERSE REACTIONS (6)** section, **Postmarketing Experience with the Individual Components of Omeclamox-Pak (6.3)** subsection under the Omeprazole subheading, under the subheading section *Metabolism and Nutritional disorders*, has been revised to include hypomagnesemia with or without hypocalcemia and/or hypokalemia.

In addition, minor editorial revisions were made throughout the PI.

APPROVAL & LABELING

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

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 Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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).

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

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>.

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 information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety 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).

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 Christopher L. Smith, PharmD, MPH, Regulatory Project Manager at (301) 796-4851.

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(S):

- 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
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