NDA 50824/S-009

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 June 26, 2020, and your amendments, 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 June 18, 2020, 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 acute tubulointerstitial nephritis associated with PPIs leading to chronic renal inflammation and reduced renal function, reported in published literature.

This supplemental new drug application provides for revisions to the labeling for OMECLAMOX-PAK. The agreed upon changes to the language in Warnings and Precautions included in our June 18, 2020 letter are as follows (additions are noted by underline and deletion are noted by ~~strikethrough~~).

Other edits to reflect the changes are included in the following sections in the attached Prescribing Information (PI): **HIGHLIGHTS**, **CONTRAINDICATIONS (4)** section, **Hypersensitivity (4.1)** subsection, **ADVERSE RECATIONS (6)** section, and **PATIENT COUNSELING INFORMATION (17)** section.

5.6 Acute Tubulointerstitial Nephritis
Acute tubulointerstitial nephritis (TIN) has been observed in patients taking PPIs including omeprazole, a component of OMECLAMOX-PAK. TIN may occur at any point during PPI therapy.

Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions, to non-specific symptoms of decreased renal function (e.g., malaise, nausea, anorexia). In reported case series, some patients were diagnosed on biopsy and in the absence of extra-renal manifestations (e.g., fever, rash or arthralgia).

Discontinue OMECLAMOX-PAK and evaluate patients with suspected acute TIN *[see Contraindications (4.1)]*.

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.

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.

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

[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.

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).

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}

Sumathi Nambiar, M.D., M.P.H.
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/

SUMATHI NAMBIAR
11/27/2020 09:38:53 AM