NDA 209570/S-001

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Chemo Research, S.L.
c/o Exeltis USA, Inc.
Attention: Sandy S. Suh, Pharm.D.
Head, Regulatory Affairs (R&D)
180 Park Road, Suite 101
Florham Park, NJ 07932

Dear Dr. Suh:

Please refer to your supplemental new drug application (sNDA) dated June 4, 2019, received June 4, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Benznidazole tablets, 100 mg and 12.5 mg.

This Prior Approval supplemental new drug application provides for the deletion of the word eosinophilic and replacement with 'drug reaction with eosinophilia and systemic symptoms (DRESS) in the **WARNINGS AND PRECAUTIONS (5)** section, **Hypersensitivity Skin Reactions (5.3)** subsection, **ADVERSE REACTIONS (6)** section, and **Postmarketing Experience (6.2)** subsection in your product labeling as requested in the Agency's supplement request letter dated May 6, 2019.

Additionally, changes have been made to the following sections of the product labeling:

- **CONTRAINDICATIONS (4)**: removal of the alcohol and propylene glycol contraindications
- **DRUG INTERACTIONS (7)**: explanation for why the alcohol and propylene glycol contraindications were removed
- **USE IN SPECIFIC POPULATIONS (8)**: minor editorial changes
- **CLINICAL PHARMACOLOGY (12)**: summary descriptions of the results of the absorption, distribution, metabolism, and excretion (ADME) study
- **NONCLINICAL TOXICOLOGY (13)**: summary description of a male fertility study in rats
- **PATIENT COUNSELING INFORMATION (17)**: removal of the interaction with alcohol.

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 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).

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submissions dated January 16, and March 26, 2019, containing the final report and an addendum to the report for the following postmarketing requirement listed in the August 29, 2017, approval letter.

3247-2 Conduct a human absorption, distribution, metabolism, and excretion (ADME)/mass balance study to evaluate the routes and rates of benznidazole excretion, ascertain whether benznidazole has circulating drug metabolites, and if identified evaluate the routes and rates of excretion for benznidazole metabolites

[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.

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

We remind you that there is a postmarketing requirement listed in the August 29, 2017, approval letter that is still open.

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 Mr. Gregory DiBernardo, Regulatory Project Manager, at (301) 796-4063.

Sincerely,

{See appended electronic signature page}

Joseph Toerner, M.D., M.P.H.
Deputy Director for Safety
Division of Anti-Infectives
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE:

- Package Insert

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/

JOSEPH G TOERNER
11/07/2019 03:46:00 PM