CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

203284Orig1s000

Trade Name: RAVICTI Oral Liquid, 1.1 grams/ml.

Generic Name: glycerol phenylbutyrate

Sponsor: Hyperion Therapeutics Inc.

Approval Date: February 1, 2013

Indications: This new drug application provides for the use of RAVICTI (glycerol phenylbutyrate) Oral Liquid, 1.1 grams/ml, for use as a nitrogen-binding adjunctive therapy for chronic management of adult and pediatric patients ≥2 years of age with urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone. RAVICTI must be used with dietary protein restriction and, in some cases, dietary supplements (eg, essential amino acids, arginine, citrulline, protein-free calorie supplements).

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203284

NDA APPROVAL

Hyperion Therapeutics Inc.
601 Gateway Boulevard
Suite 200
South San Francisco, CA 94080

Attention: Klara Dickinson
Sr. VP Regulatory Affairs

Dear Ms. Dickinson:

Please refer to your New Drug Application (NDA) dated December 23, 2011, received December 23, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for RAVICTI (glycerol phenylbutyrate) Oral Liquid, 1.1 grams/ml.

We acknowledge receipt of your amendments dated February 22, 2012; March 13, 23, and 27, 2012; April 20, 2012; June 29, 2012; July 3 and 5, 2012; August 23, 2012; December 7, 13, 28, and 31, 2012; January 1, 8, and 23, 2013.

This new drug application provides for the use of RAVICTI (glycerol phenylbutyrate) Oral Liquid, 1.1 grams/ml, for use as a nitrogen-binding adjunctive therapy for chronic management of adult and pediatric patients ≥2 years of age with urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone. RAVICTI must be used with dietary protein restriction and, in some cases, dietary supplements (eg, essential amino acids, arginine, citrulline, protein-free calorie supplements).

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 text.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide). 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*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE-CONTAINER LABELS

We acknowledge your December 31, 2012, submission containing final printed carton and container labels.

ADVISORY COMMITTEE

Your application for Ravicti (glycerol phenylbutyrate) was not referred to an FDA advisory committee because this drug is not first in class; the application did not raise significant safety or efficacy issues that were unexpected for a drug of this class; outside expertise was not necessary and there were no controversial issues that would benefit from advisory committee discussion.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of neurologic toxicity related to the use of Ravicti (glycerol phenylbutyrate) in pediatric patients

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