



NDA 021232/S-23
NDA 206356/S-06

SUPPLEMENT APPROVAL

Swedish Orphan Biovitrum AB
Attention: Matthew Boyd
Vice President, Regulatory, North America
890 Winter Street, Suite 200
Waltham, MA 02451

Dear Mr. Boyd:

Please refer to your Supplemental New Drug Applications dated April 26, 2018 and received on April 27, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Orfadin (nitisinone) capsules and oral suspension.

This Prior Approval supplemental new drug application provides for updates to the Warnings and Precautions, Drug Interactions, and Clinical Pharmacology sections of the Prescribing Information regarding a new safety signal of asymptomatic keratopathies identified post-marketing. In addition, results of *in vitro* and *in vivo* drug interaction studies evaluating nitisinone were added, including, but not limited to, inhibition of CYP2C9 and OAT1/3 and induction of CYP2E1 by nitisinone.

APPROVAL & LABELING

We completed our review of the supplemental 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 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at:

<http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 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.

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, contact LCDR Hong Vu, Regulatory Project Manager, at (301) 796-7401.

Sincerely,

{See appended electronic signature page}

Lisa Soule, MD
Associate Director
Division of Gastroenterology and Inborn Errors
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:

Content of Labeling - Prescribing Information, Instructions for Use

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/

LISA M SOULE
05/17/2019 09:50:31 AM