



NDA 022181/S-018
NDA 205065/S-007

SUPPLEMENT APPROVAL

BioMarin Pharmaceutical Inc.
Attention: Elizabeth A. Moyle
Executive Director, Regulatory Affairs Global Labeling
105 Digital Dr.
Novato, CA 94949

Dear Ms. Moyle:

Please refer to your supplemental new drug applications (sNDA) dated and received February 22, 2019 (022181/S-018) and October 28, 2019 (205065/S-007) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Kuvan (sapropterin dihydrochloride) tablets and Kuvan (sapropterin dihydrochloride) powder for oral solution.

We acknowledge receipt of your amendments dated May 15, 2019, August 28, 2019, September 26, 2019, and December 12, 2019.

This Prior Approval supplemental new drug application expands the Warnings and Precautions section 5.2 from "Gastritis" to "Upper Gastrointestinal Mucosal Inflammation" and adds "esophagitis" to the Adverse Reactions, Postmarketing Experience subsection of the Prescribing Information.

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 with minor editorial revisions listed below and reflected in the enclosed labeling.

- Update the revision date at the end of Highlights in the Prescribing Information and at the end of the Patient Information to the approval month.

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 and Patient Package Insert, , 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).

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 CAPT Mimi Phan, Regulatory Project Manager, at 301-796-5408.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, MD, MPH
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors
Products
Office of Drug Evaluation III

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>.

Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert
 - 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/

JOYCE A KORVICK
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