DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205065/S-002

SUPPLEMENT APPROVAL

BioMarin Pharmaceutical Inc.
Attention: Elizabeth Moyle
Senior Director Regulatory Affairs Global Labeling
105 Digital Drive
Novato, CA 94949

Dear Ms. Moyle:

Please refer to your Supplemental New Drug Application (sNDA) dated and received July 8, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Kuvan (sapropterin dihydrochloride) Powder for Oral Solution.

This "Changes Being Effected" supplemental new drug application proposes to update NDA 205065 with the same changes (below) that were approved for NDA 22181/S-014 (Kuvan Tablet formulation) on June 13, 2016.

- Inclusion of data from recently completed in vitro drug interaction studies (Section 7 Drug Interactions, Section 12.3 Pharmacokinetics, and Section 17 Patient Counseling Information)
- Addition of a new safety term "rhinitis" (Section 6 Adverse Reactions)
- Inclusion of the chemical structure of sapropterin dihydrochloride in Section 11 Description (the chemical structure was inadvertently deleted from the PI in the approval of NDA 22181/S-014).

APPROVAL & LABELING

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

We note that your June 27, 2016, submission includes final printed labeling (FPL) for your package insert and Instructions for Use. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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, 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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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 Heather Buck, Regulatory Project Manager, at (301) 796-1413.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOYCE A KORVICK
08/09/2016