BLA 125164/S-089

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Vifor (International) AG
c/o ProPharma Group
Attention: Ayesha Adil, US Agent
Director, Regulatory Program Management
1129 20th St, NW, Suite 600
Washington, DC 20036

Dear Ayesha Adil:

Please refer to your supplemental biologics license application (sBLA), dated and received June 30, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Mircera (methoxy polyethylene glycol-epoetin beta) injection.

This Prior Approval sBLA provides for extension of the indication for the treatment of anemia associated with chronic kidney disease (CKD) in pediatric patients 3 months to 17 years of age on dialysis and not on dialysis who are converting from another erythropoiesis-stimulating agent (ESA) after their hemoglobin level was stabilized with an ESA. Previously, the indication was approved for pediatric patients 5 to 17 years of age with CKD on hemodialysis. Additionally, this Prior Approval sBLA provides for a subcutaneous route of administration for pediatric patients. Previously, the pediatric patients could only use the intravenous route of administration.

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.

WAIVER OF HIGHLIGHTS ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling

[21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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 via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have fulfilled the pediatric study requirements for the treatment of anemia associated with CKD in pediatric patients 3 months to less than 18 years of age on dialysis or not yet on dialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submission dated October 31, 2022, containing the final reports for the following postmarketing requirements listed in the June 7, 2018, approval letter for BLA 125164/S-078.

[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.

3385-1 Conduct a multi-center, single-arm, clinical trial to confirm the dosing of US-licensed Mircera given subcutaneously in pediatric patients with anemia associated with chronic kidney disease on peritoneal dialysis or not yet on dialysis. The trial will be open to enroll pediatric patients 1 year to less than 18 years of age. The trial will evaluate maintenance of hemoglobin concentration, pharmacokinetics, and safety. The sample size will be a minimum of 40 patients (Protocol NH19708).

3385-2 Submit a summary report and registry data that describes the dosing, aggregate level safety data and hemoglobin concentrations in a cohort of pediatric patients with anemia associated with chronic kidney disease treated with US-licensed Mircera. The cohort will include pediatric patients from 3 months to less than 18 years of age, on peritoneal dialysis or hemodialysis, and subcutaneous or intravenous route of administration. The sample size for the cohort will be a minimum of 125 patients.

We have reviewed your submission and conclude that the above requirements were fulfilled.

This completes all of your postmarketing requirements acknowledged in our June 7, 2018, letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMC in your annual report required under 21 CFR 601.70 of the FD&CA.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

If you have any questions, contact Courtney Hamilton, Regulatory Project Manager at 301-796-6849 or at Courtney.Hamilton@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Ann Farrell, MD
Division Director
Division of Nonmalignant Hematology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - 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/

ANN T FARRELL
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