DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125164/S-078

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT
RELEASE FROM POSTMARKETING REQUIREMENT
NEW POSTMARKETING REQUIREMENT

Vifor International AG
c/o Biologics Consulting Group, Inc.
Attention: Kelly Boyle
Authorized US Agent for Vifor (International) Inc.
1555 King Street, Suite 300
Alexandria, VA 22314

Dear Ms. Boyle:

Please refer to your Supplemental Biologics License Application (sBLA), dated December 14, 2017, received December 14, 2017, and your amendments, submitted under section 351(a) of the Public Health Service Act for Mircera® (methoxy polyethylene glycol-epoetin beta) Solution for Injection.

We also refer to our approval letter dated June 7, 2018 which contained the following error: The PMR Set Number 3885 was incorrect. The set number should be 3385.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain June 7, 2018 the date of the original approval letter.

This Prior Approval supplemental biologics application provides for a new indication for Mircera administered by intravenous route for the treatment of anemia associated with chronic kidney disease (CKD) in pediatric patients 5 to 17 years of age on hemodialysis who are converting from another erythropoiesis-stimulating agent (ESA) after their hemoglobin level was stabilized with an ESA.

APPROVAL & LABELING

We have completed our review of this 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.

WAIVER OF HIGHLIGHTS SECTION

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the prescribing information, text for 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

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 MS Word format that includes the changes approved in this supplemental application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submissions dated August 12, 2016, and December 14, 2017, containing the final reports for the following postmarketing requirement listed in the November 14, 2007, approval letter for BLA 125164.

PMR 2471-1 To conduct a multi-center, dose-finding study to determine the optimum starting dose of intravenously administered methoxy polyethylene glycol-epoetin beta when used for the maintenance treatment of anemia in pediatric patients ages 5 to 17 years who have chronic kidney disease and are undergoing dialysis.

We have reviewed your submission and conclude that the above requirement was fulfilled.

RELEASE FROM POSTMARKETING REQUIREMENT

We have received your submissions dated August 12, 2016, and December 14, 2017, reporting on the following postmarketing requirement listed in our November 14, 2007, approval letter:

PMR 2471-2 To conduct a multi-center, randomized, controlled, parallel-group study to confirm the optimal methoxy polyethylene glycol-epoetin beta dosage when used for the maintenance treatment of anemia in pediatric patients ages 5 to 17 years

who have chronic kidney disease, inclusive of patients undergoing dialysis as well as patients who are not undergoing dialysis.

We have reviewed your submission and have determined that you are released from the above postmarketing requirement because the original study for PMR 2471-2 is no longer feasible due to the limited number of pediatric patients that would be available to enroll in the original randomized trial design. The Agency agrees with your updated pediatric development plan submitted to BLA 125164 on February 17, 2017, to conduct a single-arm multicenter trial and a registry study in pediatric patients with CKD treated with US-licensed Mircera.

We remind you that there is a postmarketing commitment listed in the November 14, 2007, approval letter that is still open.

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.

We note that you have fulfilled the pediatric study requirement for the treatment of anemia associated with CKD in pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.

Your deferred pediatric studies required under section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 601.70 and section 505B(a)(3)(C) of the FDCA. These required studies are listed below.

PMR 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).

Trial Completion:	10/2021
Final Report Submission:	10/2022

PMR 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.

Final Report Submission: 10/2022

Reports of these required pediatric postmarketing studies must be submitted as biologics license application (BLA) or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the prescribing information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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).

If you have any questions, call Michael Gwathmey, Regulatory Project Manager, at (301) 796-8498.

Sincerely,

{See appended electronic signature page}

R. Angelo de Claro, MD
Acting Deputy Director
Division of Hematology Products
Office of Hematology and Oncology Products
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/

ROMEO A DE CLARO
06/07/2018