



BLA 761088/S-005
BLA 761088/S-006

SUPPLEMENT APPROVAL

Celltrion, Inc.
c/o Parexel International Corporation
4600 East-West Highway, Suite 350
Bethesda, MD 20814

Attention: Ryan Zettle, PharmD, MBA
Senior Consultant, Parexel Consulting

Dear Dr. Zettle:

Please refer to your supplemental biologics license application (sBLA), dated June 27, 2019, received June 27, 2019, and your amendments, submitted under section 351(k) of the Public Health Service Act for Truxima (rituximab-abbs) injection, 500 mg/50 mL, 100 mg/10 mL.

These Prior Approval supplemental biologics license applications provide for the addition of the following indications:

- Supplement 005 – Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to severely-active RA who have inadequate response to one or more TNF antagonist therapies,
- Supplement 006 – Granulomatosis with Polyangiitis (GPA) Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult patients in combination with glucocorticoids.

APPROVAL & LABELING

We have completed our review of these supplemental applications. They are 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 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.

Supplement S-005: Rheumatoid Arthritis

At this time, we have determined that, with respect to this indication, no pediatric studies will be required under PREA for your supplemental BLA.

Supplement S-006: Granulomatosis with Polyangiitis and Microscopic Polyangiitis

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>.

At this time, we have determined that, with respect to GPA and MPA in pediatric patients 0 to less than 2 years of age, no pediatric studies will be required under PREA for your supplemental BLA.

We are deferring submission of your pediatric assessment for Supplement S-006 for the GPA and MPA indications for patients 2 years of age and older. See Deferred Pediatric Assessment below.

Deferred Pediatric Assessment

Your deferred pediatric study(ies) required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act is required postmarketing study(ies). The status of this/these postmarketing study(ies) must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act. This required assessment is listed below.

3772-1: Assessment of Truxima (rituximab-abbs) for the treatment of Granulomatosis with Polyangiitis and Microscopic Polyangiitis in pediatric patients 2 years of age and older.

The timetable you submitted on December 16, 2019, states that you will conduct this assessment according to the following schedule:

Final Report Submission: 9/2026

Reports of this/these required pediatric postmarketing study(ies) must be submitted as a 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, please 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

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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 *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

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 FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁶

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 Susan Rhee, Regulatory Project Manager, at 301-796-2402.

Sincerely,

{See appended electronic signature page}

Sally Seymour, MD
Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling

- Prescribing Information
- Medication Guide

³ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-prescription-drug-promotion-opdp>

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/

NIKOLAY P NIKOLOV

12/18/2019 04:05:07 PM

Signed under the authority delegated by Dr. Sally Seymour, Division Director, DPARP.