

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761354Orig1s000

Trade Name: Tofidence

Generic or Proper Name: (tocilizumab-bavi) injection

Sponsor: Biogen MA Inc.

Approval Date: 9/29/23

Indication: treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis (PJIA) in 2 years of age and older, and systemic juvenile idiopathic arthritis (SJIA) in 2 years of age and older.

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APPROVAL LETTER



BLA 761354

BLA APPROVAL

Biogen MA Inc.
225 Binney Street
Cambridge, MA 02142

Attention: Lauren Seabrook
Associate Director, US Regulatory Lead

Dear Lauren Seabrook:

Please refer to your biologics license application (BLA) dated and received September 29, 2022, and your amendments, submitted under section 351(k) of the Public Health Service Act for Tofidence (tocilizumab-bavi), injection 80 mg/4 mL, 200 mg/10 mL, and 400 mg/20 mL.

BLA 761354 provides for the use of Tofidence (tocilizumab-bavi) in treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis (PJIA) in 2 years of age and older, and systemic juvenile idiopathic arthritis (SJIA) in 2 years of age and older.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2344 to Biogen MA Inc., Cambridge, MA, under the provisions of section 351(k) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Tofidence (tocilizumab-bavi). Tofidence is indicated for the indications listed above.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture tocilizumab-bavi drug substance and the final formulated drug product at [REDACTED] (b) (4). You may label your product with the proprietary name, Tofidence, and market it in 80mg/4mL (20mg/mL), 200mg/10mL (20mg/mL), and 400mg/20mL (20mg/mL) single-dose vials for further dilution prior to intravenous infusion.

DATING PERIOD

The dating period for Tofidence shall be 24 months from the date of manufacture when stored at 2°C to 8°C, protected from light. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4)°C.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Tofidence to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Tofidence, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

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 ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, and Medication Guide). Information on submitting SPL files using eLIST may be found in the

¹ See <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

guidance for industry *SPL Standard for Content of Labeling Technical Qs and As (October 2009)*.²

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved BLA 761354.**” Approval of this submission by FDA is not required before the labeling is used.

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.

The following comment pertains to the Polyarticular Juvenile Idiopathic Arthritis (PJIA) indication:

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

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

- 4510-1 To implement [REDACTED] (b) (4) of the sterile filter during sterile filtration.

The timetable you submitted on August 18, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/2024

- 4510-2 To implement revised procedure with target flushing volume of $\geq$ [REDACTED] (b) (4) L for post-use filter integrity test

The timetable you submitted on August 10, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/2024

Submit clinical protocols to your IND 142381 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment Protocol**,” “**Postmarketing Commitment Final Report**,” or “**Postmarketing Commitment Correspondence**.”

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

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

[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

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

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

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

If you have any questions, call Susie Choi, Regulatory Project Manager, at 240-402-2925.

Sincerely,

{See appended electronic signature page}

Rachel Glaser, MD
Associate Director for Therapeutic Review
Division of Rheumatology and Transplant Medicine
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Medication Guide
- Carton and Container Labeling

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/

RACHEL GLASER
09/29/2023 11:14:40 AM