

BLA 761225

**BLA APPROVAL**

Hugel, Inc  
c/o Strategic Drug Development Services, LLC  
Attention: Scott A. Oglesby, PhD  
Executive Consultant  
6518 Green Rise Road  
Hillsborough, NC 27278

Dear Dr. Oglesby:

Please refer to your biologics license application (BLA) dated and received March 31, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for Letybo (letibotulinumtoxinA-wlbg) for injection, for intramuscular use.

We acknowledge receipt of your resubmission dated August 31, 2023, which constituted a complete response to our April 12, 2023, action letter.

### **LICENSING**

We are issuing Department of Health and Human Services U.S. License No. 2237 to Hugel, Inc, Chuncheon, Gangwon, Korea under the provisions of section 351(a) 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 Letybo (letibotulinumtoxinA-wlbg) for injection, for intramuscular use indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients.

### **MANUFACTURING LOCATIONS**

Under this license, you are approved to manufacture letibotulinumtoxinA-wlbg at your facility in Chuncheon-si, Gangwon-do, Republic of Korea. You may label your product with the proprietary name, Letybo, and market it in 50 Units/vial or 100 Units/vial for injection.

## **DATING PERIOD**

The dating period for Letybo shall be 36 months from the date of manufacture when stored at 2- 8 °C. 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.

## **FDA LOT RELEASE**

You are not currently required to submit samples of future lots of Letybo 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 Letybo, 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 with minor editorial revisions listed below and reflected in the enclosed labeling.

- 1) **HIGHLIGHTS OF PRESCRIBING INFORMATION** section
  - a) Update the **Initial U.S. Approval** to **2024**.
  - b) Update the **Revised** date to **03/2024**.
- 2) **FULL PRESCRIBING INFORMATION** section
  - a) Update U.S. License Number to 2237.
  - b) Update © to 02/2024 or your preferred format.
- 3) **MEDICATION GUIDE**
  - a) Update U.S. License No, to 2237.
  - b) Update the Issued date to 02/2024.
  - c) Update © to 02/2024 or your preferred format.

## **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.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and

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<sup>1</sup> See <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>  
U.S. Food and Drug Administration  
Silver Spring, MD 20993  
[www.fda.gov](http://www.fda.gov)

Medication Guide). 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 (October 2009)*.<sup>2</sup>

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 761225.**” Approval of this submission by FDA is not required before the labeling is used.

### **ADVISORY COMMITTEE**

Your application for Letybo was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues that were unexpected for a biologic of this class.

### **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 are waiving the pediatric study(ies) requirement for this application because necessary studies are impossible or highly impracticable in patients less than age 18 years of age.

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

We remind you of your postmarketing commitments:

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<sup>2</sup> 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>.

- 4587-1 To investigate the development and implementation of a non-animal based potency assay for drug substance and drug product release and stability testing

The timetable you submitted on February 22, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2028

Submit clinical protocols to your IND 123178 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*.<sup>3</sup>

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](http://FDA.gov).<sup>4</sup> Information and Instructions for completing the form can be found at [FDA.gov](http://FDA.gov).<sup>5</sup>

### **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.

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

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

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

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

### **POST APPROVAL FEEDBACK MEETING**

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, email H. F. Van Horn III, PharmD, MBA, Regulatory Project Manager, at [Howard.VanHornIII@fda.hhs.gov](mailto:Howard.VanHornIII@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Nikolay P. Nikolov, MD  
Acting Office Director  
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 Label

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**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.**  
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/s/  
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