CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761127Orig1s000

Trade Name:	Daxxify for injection.
Generic or Proper Name:	daxibotulinumtoixnA-lanm
Sponsor:	Revance Therapeutics, Inc.
Approval Date:	September 7, 2022
Indication:	for the treatment of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients.

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761127Orig1s000

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APPROVAL LETTER

BLA 761127

BLA APPROVAL

Revance Therapeutics, Inc.
Attention: Michelle Frazier, PhD
Vice President, Global Regulatory Affairs
7555 Gateway Blvd.
Newark, CA 94560

Dear Dr. Frazier:

Please refer to your biologics license application (BLA) dated November 24, 2019, received November 25, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for Daxxify (daxibotulinumtoixnA-lanm) for injection.

We acknowledge receipt of your resubmission dated March 8, 2022, which constituted a complete response to our October 14, 2022, action letter.

LICENSING

We have approved your BLA for Daxxify (daxibotulinumtoixnA-lanm) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Daxxify under your existing Department of Health and Human Services U.S. License No. 2101. Daxxify is indicated for the treatment 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 daxibotulinumtoixnA-lanm at the Revance Therapeutics, Inc. facility in Newark, California. The packaging and labeling of finished drug product will be performed at (b) (4) You may label your product with the proprietary name, Daxxify, and market it in 50 Units or 100 Units sterile lyophilized powder in a single-dose vial for injection.

DATING PERIOD

The dating period for Daxxify shall be months 24 months for the 50 Units/vial and 12 months for the 100 Units/vial strengths from the date of manufacture when stored at 20-25 °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.

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

FDA LOT RELEASE

While your product qualifies for the lot release program, FDA granted an exception and you are not currently required to submit samples of future lots of Daxxify 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 Daxxify, or in the manufacturing facilities, will require the submission of information to your biologics license application 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.

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 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

[1] See 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 at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761127**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for daxibotulinumtoixnA-lanm 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:

761127-01

To develop, validate, and implement an appropriate host cell protein assay to monitor and control for *Clostridium botulinum*-derived process impurities in daxibotulinumtoxinA drug substance either as a release specification with adequate acceptance criteria or as an inprocess test with appropriate rejection limits. The final study report, along with updated drug substance control strategy, will be submitted in accordance with 21 CFR 601.12.

Final Report Submission 12/17/2022

761127-02

To develop, validate, and implement an appropriate cell-based potency assay to replace the current in vivo mouse LD50 potency assay for the release and stability testing of daxibotulinumtoxinA drug substance and drug product.

The final study report, along with updated drug substance and drug product control strategy, will be submitted in accordance with 21 CFR 601.12.

Final Report Submission 03/31/2024

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 129198 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 [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.

[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

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, call Kimberle Searcy, Regulatory Project Manager, at 240-402-4454.

Sincerely,

{See appended electronic signature page}

Julie G. Beitz, MD
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 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/

JULIE G BEITZ
09/07/2022 12:49:46 PM