BLA 761146

BLA APPROVAL

Endo Global Aesthetics Limited
c/o Endo Pharmaceuticals Inc.
Attn: Erin Abdallah
Associate Director, Regulatory Affairs
1400 Atwater Drive
Malvern, PA 19355

Dear Ms. Abdallah:

Please refer to your biologics license application (BLA) dated and received September 6, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for Qwo (collagenase clostridium histolyticum-aaes) for injection.

LICENSING

We have approved your BLA for Qwo (collagenase clostridium histolyticum-aaes) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Qwo under your existing Department of Health and Human Services U.S. License No. 2136. Qwo is indicated for the treatment of moderate to severe cellulite in the buttocks of adult women.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture collagenase clostridium histolyticum-aaes drug substance at (b) (4) (b) (4) The final formulated drug product and sterile diluent will be manufactured, filled, labeled, and packaged at (b) (4) (b) (4) The final formulated drug product and sterile diluent may also be packaged at (b) (4) You may label your product with the proprietary name, Qwo, and market it in 0.92 mg for reconstitution in 4 mL of sterile diluent for one treatment area, and 1.84 mg for reconstitution in 8 mL of sterile diluent for two treatment areas.

DATING PERIOD

The dating period for Qwo shall be 24 months from the date of manufacture when stored at 2 to 8°C. The dating period for the sterile diluent shall be 24 months from the date of manufacture when stored at (b) (4) °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.

The expiration date for the packaged product, Qwo (collagenase clostridium histolyticum-aaes) plus sterile diluent shall be dependent on the shortest expiration date of any component.

Results of ongoing stability studies should be submitted throughout the dating period, as they become available, including the results of stability studies from the first three production lots.

We have approved the stability protocol(s) in your license application for the purpose of extending the expiration dating period of your drug substance, drug product, and sterile diluent under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Qwo and each kit component 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 Qwo, 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, as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (Prescribing Information, and Patient Package Insert). Information on submitting SPL files using

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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.

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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761146**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for collagenase clostridium histolyticum was not referred to an FDA advisory committee because collagenase clostridium histolyticum is an approved product for other indications. The safety profile in the target population with moderate to severe cellulite in the buttocks of adult women was expected to be similar to the safety profile in the populations for which the product is approved.

REQUIRED PEDIATRIC ASSESSMENTS

We are waiving the pediatric study(ies) requirement for this application because studies are impossible or highly impracticable since the estimated number of patients with moderate to severe cellulite less than age 18 years is extremely small.

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

We remind you of your postmarketing commitments:

3867-1 Conduct a drug product (DP) transport qualification study shipping 5 mL and 10 mL vials of CCH Mannitol DP from (b) (4) to the (b) (4) packaging site in (b) (4)

The timetable you submitted on May 14, 2020, states that you will conduct this study according to the following schedule:

[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.

Final Report Submission: 06/21

3867-2 The target filtration volume of (b) (4) mL was not achieved for one of the test filters (lot number: R6EA67189) in the bacterial retention study due to (b) (4)
Conduct a bacterial retention study to simulate the target filtration volume and maximum flow rate throughout the study duration for all test filters.

The timetable you submitted on May 14, 2020, states that you will conduct this study according to the following schedule:

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3867-3 The validation runs (b) (4) (refer to table IX in the "Manufacturing Equipment Validation Summary - Lyophilized Powder" document in section P.3.5). In response to the Agency's IR dated May 6, 2020, (b) (4) Provide data summaries from recent validation runs (b) (4)

The timetable you submitted on May 14, 2020, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/21

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]

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

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 for licensed biological products (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 for licensed biological products (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

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at FDA.gov.[6]

POST APPROVAL FEEDBACK MEETING

New molecular entities and 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 Craig Johnson, Regulatory Project Manager, at 301-796-3921.

Sincerely,

{See appended electronic signature page}

Kendall A. Marcus, MD
Director
Division of Dermatology and Dentistry
Office of Immunology and Inflammation
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

[6] http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm

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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.

/s/

KENDALL A MARCUS
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