



BLA 103846/S-5190

SUPPLEMENT APPROVAL

Solstice Neurosciences, LLC
o/b/o US WorldMeds, LLC
Attention: Adam Reuther, Director of Regulatory Affairs
4441 Springdale Rd.
Louisville, KY 40241

Dear Mr. Reuther:

Please refer to your supplemental biologics license application (sBLA), dated and received October 30, 2018, and your amendments, submitted under section 351(a) of the Public Health Service Act for Myobloc (rimabotulinumtoxinB) injection.

This Prior Approval supplemental biologics application provides for a new indication for the treatment of sialorrhea in adults.

APPROVAL & LABELING

We have completed our review of this application. 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 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 Effectuated” (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.

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>.

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.

We are waiving the pediatric studies requirement for patients ages 0 to less than 3 years because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group and is not likely to be used in a substantial number of pediatric patients in this group. In this age group, drooling may be normal, and a potential benefit from treatment appears unlikely.

We are deferring submission of your pediatric studies for ages 3 to 17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

3687-1 A randomized, double-blind, placebo-controlled, dose-response study in pediatric subjects 3 to less than 17 years of age with chronic troublesome sialorrhea. Subjects will be randomized to receive a single injection session of low-dose Myobloc, high-dose Myobloc, or placebo. Children ages 6 to less than 17 years of age will be enrolled first.

The timetable you submitted on August 15, 2019, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	Submitted 11/2017
Final Protocol Submission:	12/2019
Study/Trial Completion:	06/2023
Final Report Submission:	12/2023

3687-2 A long-term, open-label safety and efficacy study in pediatric subjects 3 to less than 17 years of age with chronic troublesome sialorrhea that will follow the randomized, double-blind, placebo-controlled study. The long-term safety study needs to include information from at least 100 patients treated with Myobloc for chronic sialorrhea for 4 consecutive treatments over approximately 1-year, with at least 50 of these patients treated with the highest dose of Myobloc recommended in the label. Submit an interim report for the long-term safety study, for safety information from pediatric patients ages 6 to < 17-years-old treated with Myobloc for sialorrhea for 4 consecutive treatments.

The timetable you submitted on August 15, 2019, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	Submitted 11/2017
Final Protocol Submission:	12/2019
Interim Report:	12/2023
Study/Trial Completion:	06/2024
Final Report Submission:	12/2024

A final protocol is considered to be an agreed-upon protocol 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 the protocols to your IND 100454, with a cross-reference letter to this BLA.

Reports of these required pediatric postmarketing studies must be submitted as a 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.

We remind you that there are postmarketing requirements and commitments listed in the April 29, 2009, approval letter that are still open.

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
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

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 <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

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, contact Brenda Reggetz, PharmD, Regulatory Health Project Manager, by email at Brenda.Reggetz@fda.hhs.gov or by phone at (240) 402-6220.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Acting Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Medication Guide

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/

ERIC P BASTINGS
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