

BLA 125360/S-086
BLA 125360/S-092

SUPPLEMENT APPROVAL

Merz Pharmaceuticals GmbH
Attention: Hadley Iliff, MA, MBA
Director, US Regulatory Affairs
6501 Six Forks Road
Raleigh, NC 27615

Dear Ms. Iliff:

Please refer to the following supplemental biologics license applications (sBLAs), and your amendments, submitted under section 351(a) of the Public Health Service Act for Xeomin (incobotulinumtoxinA) injection:

1. **sBLA 125360/086**

This Prior Approval supplemental biologics application dated June 16, 2020, received June 18, 2020, provides for the addition of the following indication: treatment of chronic sialorrhea in patients 2 years of age and older.

2. **sBLA 125360/092**

This Changes Being Effected supplemental biologics application dated October 28, 2020, received October 28, 2020, provides for a modification of Table 3 (Xeomin Dosing by Muscle for Treatment of Pediatric Upper Limb Spasticity, Excluding Spasticity Caused by Cerebral Palsy) in Section 2.3 of the Prescribing Information for Xeomin, to reflect the correct number of injection sites per muscle for the pronator quadratus and pronator teres muscles.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF HIGHLIGHTS ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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 Effected” (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.

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 FOR sBLA 125360/086

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.

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>.

FULFILLMENT OF POSTMARKETING REQUIREMENT FOR sBLA 125360/086

We have reviewed your submission dated June 16, 2020, reporting on the following postmarketing requirement listed in the July 3, 2018, approval letter for sBLA 125360/073.

3443-1 A double-blind, parallel-group, placebo-control study in patients ages 6 to 17 years, and an open-label, single-group, non-controlled study in patients ages 2 to 5 years conducted under PREA to evaluate the efficacy and safety of Xeomin for treatment of chronic troublesome sialorrhea in the pediatric population. This will be followed by an open-label extension period to investigate the safety of repeat dosing of Xeomin for the treatment of pediatric patients (2-17 years) with chronic troublesome sialorrhea.

We have reviewed your submission and conclude that the above requirement was fulfilled.

We note that you have fulfilled the pediatric study requirement for all relevant pediatric age groups for this application.

We remind you that there are postmarketing requirements and commitments listed in the July 30, 2010, approval letter that are still open.

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

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

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).

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>

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If you have any questions, contact Taura Holmes, PharmD, MS, Senior Regulatory Project Manager, at Taura.Holmes@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Director (Acting)
Division of Neurology 1
Office of Neuroscience
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
12/18/2020 08:31:45 AM