DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125360/S-045

SUPPLEMENT APPROVAL

Merz Pharmaceuticals LLC
Attention: Jason Mercer
Regulatory Affairs Manager
4215 Tudor Lane
Greensboro, NC 27410

Dear Dr. Mercer:

Please refer to your Supplemental Biologics License Application (sBLA), dated September 26, 2012, received September 27, 2012, submitted under section 351(a) of the Public Health Service Act for Xeomin (incobotulinumtoxinA).

We acknowledge receipt of your amendment dated October 31, 2012.

This "Changes Being Effected" labeling supplement to your biologics license application proposes the addition of the adverse event term "flu-like symptoms" to the Xeomin prescribing information under Section 6.3 – Postmarketing Experience.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the minor editorial revisions listed below.

In addition, we request you verify whether the lack of identification of "flu-like symptoms" as an adverse event in Xeomin clinical trials was not due to an inconsistent interpretation of verbatim descriptions of flu-like adverse events, and the resultant coding to MedDRA preferred terms. Please review adverse event reports in the double-blind Phase 3 Xeomin clinical trials that supported the BLA, and identify all verbatim terms that may potentially identify a case of "flu-like symptoms". Please develop an algorithm for mapping the verbatim terms to Preferred Terms (PTs) ensuring, for example, that PTs such as "*flu-like symptoms*", "*nasopharyngitis*", and "*upper respiratory tract infection*" are consistently applied. Apply that algorithm to compare the incidence of "flu-like" symptoms in the various treatment groups in your phase 3 studies, and submit the results to the Agency for review.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to, except with the revisions listed, the enclosed labeling 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes 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 MS Word format that includes the changes approved in this supplemental application.

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 package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see 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 Karen Abraham-Burrell, PharmD, Regulatory Project Manager, by phone or email at (301) 796-2721 or Karen.Abraham-Burrell@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC P BASTINGS
04/11/2013