DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103000/5232

SUPPLEMENT BLA APPROVAL
August 24, 2011

Allergan, Inc.
Attention: Gus Aromin
Director, Global Regulatory Affairs
2525 Dupont Drive
Irvine, CA 92623-9534

Dear Mr. Aromin:

Please refer to your Supplemental Biologics License Application (sBLA) dated October 26, 2010, received October 27, 2010, submitted under section 351 of the Public Health Service Act for BOTOX (onabotulinumtoxinA).

We acknowledge receipt of your amendments dated February 23, June 15, 17, and 24, and August 22, 2011, and your risk evaluation and mitigation strategy (REMS) assessment dated January 31, 2011.

This "Prior Approval" efficacy supplement to your biologics license application provides for a new indication for the treatment of adults with urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) who have an inadequate response to or are intolerant of an anticholinergic medication and a proposed modification to the approved REMS.

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.

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 the enclosed labeling (text for the package insert, text for the patient package insert, 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 titled "SPL Standard for Content of Labeling Technical Qs and As"

at
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 103000/5232.**

Also within 14 days, amend all pending supplemental applications 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.

The SPL will be accessible via publicly available labeling repositories.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages < 10 years because the adult condition (i.e. urinary incontinence due to detrusor overactivity associated with a neurologic condition) is uncommonly treated in younger children.

We are deferring submission of your pediatric study for patients ≥ 10 years to ≤ 17 years of age because this product is ready for approval for use in adults and the pediatric study has 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)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1. Pediatric study in patients ≥ 10 years to ≤ 17 years of age to evaluate the safety and efficacy of BOTOX in the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g. spina bifida or spinal cord injury).

Final Protocol Submission:	February 2012
Study Completion:	April 2017
Final Report Submission:	August 2017

2. Long-term pediatric study in patients ≥ 10 years to ≤ 17 years of age to evaluate the safety and efficacy of BOTOX in the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g. spina bifida or spinal cord injury).

Final Protocol Submission:	March 2012
Study Completion:	March 2018
Final Report Submission:	September 2018

Submit final study reports to this BLA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessments.**"

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for BOTOX (onabotulinumtoxinA) was originally approved on July 31, 2009, and a REMS modification was approved on October 15, 2010. The REMS consists of a Medication Guide, a communication plan, and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of a revised Medication Guide to include information about the new indication.

Your proposed modified REMS, submitted on August 22, 2011, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on July 31, 2009.

There are no changes to the REMS assessment plan described in our July 31, 2009, letter.

We remind you that assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved

REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 103000 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 103000
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 103000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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
Division of Drug Marketing, Advertising, and Communications
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 Division of Drug Marketing, Advertising, and Communications (DDMAC), 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, call Eufrecina DeGuia, Senior Regulatory Health Project Manager, at (301) 796-0881.

Sincerely,

George S. Benson 8/24/2011

/ George Benson, M.D. /
Deputy Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling (including Medication Guide)
REMS