



NDA 20297/S-033  
NDA 22012/S016

**SUPPLEMENT APPROVAL**

GlaxoSmithKline  
Attention: Linda Rebar  
US Regulatory Affairs  
5 Moore Drive  
Research Triangle Park, NC 27709

Dear Ms. Rebar:

Please refer to your Supplemental New Drug Applications (sNDAs) dated December 15, 2009, received December 15, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Coreg (carvedilol) 3.125 mg, 6.25 mg, 12.5 mg, and 25 mg, Tablets and Coreg CR (carvedilol phosphate) 10 mg, 20 mg, 40 mg, and 80 mg Extended Release Capsules.

We acknowledge receipt of your amendments dated June 10, 2010.

The June 10, 2010, submissions constitute a complete response to our May 18, 2010, action letter.

These "Prior Approval" supplemental new drug applications provide for changes to the **HIGHLIGHTS, WARNINGS AND PRECAUTIONS**, and **PATIENT COUNSELING INFORMATION** sections of the label and the Patient Information Leaflet.

The following changes were made to both supplements:

1. In **Highlights**, the **RECENT MAJOR CHANGES** section was updated to reflect changes to the Warnings and Precautions section for Intraoperative Floppy Iris Syndrome, which you identified placement as section 5.14.
2. Also in **Highlights Contents**, an additional section 5.14 was added for Intraoperative Floppy Iris Syndrome and an additional section 17.2 was added for FDA-Approved Patient Labeling.
3. In **WARNINGS AND PRECAUTIONS**, section 5.14 was added. It reads as follows:

**5.14 Intraoperative Floppy Iris Syndrome**

Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients treated with alpha-1 blockers (Coreg is an alpha/beta blocker). This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard midriatic drugs, and potential prolapse of the iris toward the phacoemulsification incisions. The patient's ophthalmologist should be prepared for possible modifications to the surgical technique such as utilization of iris

hooks, iris dilator rings, or viscoelastic substances. There does not appear to be a benefit of stopping alpha-1 blocker therapy prior to cataract surgery.

4. In **PATIENT COUNSELING INFORMATION**, section 17.2 was added. It reads as follows:

“Patient labeling is provided as a tear-off leaflet at the end of this full prescribing information.”

5. In the Patient Information Leaflet, the section header: **What should I tell my doctor before taking Coreg/CR?** added a bullet second from the last bullet for Coreg and third to last bullet for Coreg CR that reads:

“Are scheduled for cataract surgery and have taken or are currently taking Coreg.”

6. The revision date and version number were updated.

We have completed our review of these supplemental applications, as amended and they are 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, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] 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,) and include the labeling changes proposed in any pending “Changes Being Effectuated” (CBE) supplements and any annual reportable changes not included in the enclosed labeling. 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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

### **PROMOTIONAL MATERIALS**

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

**LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program  
Office of Special Health Issues  
Food and Drug Administration  
10903 New Hampshire Ave  
Building 32, Mail Stop 5353  
Silver Spring, MD 20993

**REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call:

Lori Anne Wachter, RN, BSN  
Regulatory Project Manager  
(301) 796-3975

Sincerely,

*{See appended electronic signature page}*

Mary Ross Southworth, Pharm.D.  
Deputy Director for Safety  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MARY R SOUTHWORTH  
01/25/2011