



NDA 20-297/S-028

GlaxoSmithKline  
Attention: Catherine Clark  
One Franklin Plaza  
200 N. 16<sup>th</sup> Street  
Philadelphia, PA 19102

## SUPPLEMENT APPROVAL

Dear Ms. Clark:

Please refer to your supplemental new drug application (NDA) dated February 4, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Coreg (carvedilol) 3.125, 6.25, 12.5, and 25 mg Tablets.

This supplemental new drug application provides for the following revisions to the package insert:

1. To delete "Warnings and Precautions, Glycemic Control in Type 2 Diabetes (5.6)" from the **RECENT MAJOR CHANGES** in the **HIGHLIGHTS OF PRESCRIBING INFORMATION** because it is beyond the 1 year period according to 201.57(a)(5).
2. To add "Both digitalis glycosides and beta-blockers slow atrioventricular conduction and decrease heart rate. Concomitant use can increase the risk of bradycardia." to the **DRUG INTERACTIONS** section of the **HIGHLIGHTS OF PRESCRIBING INFORMATION**.
3. To add a cross reference to the **INDICATIONS AND USAGE/Heart Failure section (1.1)**: "...Drug Interactions (7.4) and..."
4. To change section 7.4 of **DRUG INTERACTIONS**:

FROM

### **Digoxin**

Digoxin concentrations are increased by about 15% when digoxin and carvedilol are administered concomitantly. Both digoxin and COREG slow AV conduction. Therefore, increased monitoring of digoxin is recommended when initiating, adjusting, or discontinuing COREG [*see Clinical Pharmacology (12.5)*].

TO

### **Digitalis Glycosides**

Both digitalis glycosides and  $\beta$ -blockers slow atrioventricular conduction and decrease heart rate. Concomitant use can increase the risk of bradycardia. Digoxin concentrations are increased by about

15% when digoxin and carvedilol are administered concomitantly. Therefore, increased monitoring of digoxin is recommended when initiating, adjusting, or discontinuing COREG [*see Clinical Pharmacology (12.5)*].

5. To change “MRHD” to “maximum recommended human dose [MRHD]” in Section 8.1 **USE IN SPECIFIC POPULATIONS/Pregnancy**.
6. To add “COREG AND TILTAB are registered trademarks of GlaxoSmithKline. TOPROL-XL is a registered trademark of the AstraZeneca group of companies.” after the **PATIENT COUNSELING INFORMATION** (section 17).
7. To delete “**Rx only**” from the beginning of the patient information leaflet.
8. To make other minor editorial changes to the labeling as provided for in your submission.

We have completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon electronic labeling text. We will transmit the SPL version of the labeling submitted on February 4, 2008, with minor editorial changes, to the National Library of Medicine for public dissemination.

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH  
Food and Drug Administration  
5515 Security Lane  
HFD-001, Suite 5100  
Rockville, MD 20852

Marketing the product with labeling that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 Dan Brum, Pharm.D., Regulatory Project Manager, at (301)796-0578.

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, M.D., Ph.D.  
Director  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

cc: Enclosed Labeling Text

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Norman Stockbridge  
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