DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020297/S-036
NDA 022012/S-020

SUPPLEMENT APPROVAL

SmithKline Beecham (Cork) Ltd d/b/a GlaxoSmithKline
Attention: Linda Rebar
Director, Global Regulatory Affairs
2301 Renaissance Blvd
PO Box 61540
RN0420
King of Prussia, PA 19406-2772

Dear Ms Rebar:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received February 15, 2011, submitted under section 505(b)(1) 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 (NDA 020297) and Coreg CR (carvedilol phosphate) 10 mg, 20 mg, 40 mg, and 80 mg Extended Release Capsules (NDA 022012).

These "Changes Being Effected" supplemental new drug applications provide for labeling revised as follows:

1. Under **ADVERSE REACTIONS/Postmarketing Experience**, the second paragraph was changed from:

> Reports of aplastic anemia and severe skin reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme) have been rare and received only when carvedilol was administered concomitantly with other medications associated with such reactions. Rare reports of hypersensitivity reactions (e.g., anaphylactic reaction, angioedema, and urticaria) have been received for COREG and COREG CR®, including cases occurring after the initiation of COREG CR in patients previously treated with COREG. Urinary incontinence in women (which resolved upon discontinuation of the medication) and interstitial pneumonitis have been reported rarely.

To:

> *Blood and Lymphatic System Disorders*: Aplastic anemia.
>
> *Immune System Disorders:* Hypersensitivity (e.g., anaphylactic reactions, angioedema, urticaria).

Renal and Urinary Disorders: Urinary incontinence.

Respiratory, Thoracic and Mediastinal Disorders: Interstitial pneumonitis.

Skin and Subcutaneous Tissue Disorders: Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme.

2. The revision date and version number were updated.

There are no other changes from the last approved package insert.

We have completed our review of these supplemental applications, 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 the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as 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, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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).

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 for Safety
(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 1
Center for Drug Evaluation and Research

ENCLOSURE:
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/

MARY R SOUTHWORTH
07/06/2011