DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-297/S-017

SmithKline Beecham Corporation d/b/a GlaxoSmithKline
Attention: Ms. Catherine K. Clark
One Franklin Plaza
200 N. 16th Street
Philadelphia, PA 19102

Dear Ms. Clark:

Please refer to your electronic supplemental new drug application dated June 29, 2005, 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 changes to the **ADVERSE REACTIONS/*Postmarketing Experience*** section. In addition, minor editorial changes were made. The revisions to the draft labeling are as follows:

1. In the second paragraph of the **CLINICAL TRIALS/Trials in Mild-to-Moderate Heart Failure** section, the first sentence has been changed from:

   Four US multicenter, double-blind, placebo-controlled studies enrolled 1,094 patients (696 randomized to carvedilol) with NYHA class II-III heart failure and ejection fraction <0.35.

   To:

   Four US multicenter, double-blind, placebo-controlled studies enrolled 1,094 patients (696 randomized to carvedilol) with NYHA class II-III heart failure and ejection fraction ≤0.35.

2. In the third paragraph of the **CLINICAL TRIALS/Left Ventricular Dysfunction Following Myocardial Infarction** section, the first sentence has been changed from:

   There was also a significant 40% reduction in fatal and non-fatal myocardial infarction observed in the group treated with carvedilol (95% CI 11% to 60%, p = 0.01).

   To:

   There was also a significant 40% reduction in fatal or non-fatal myocardial infarction observed in the group treated with carvedilol (95% CI 11% to 60%, p = 0.01).

3. The **ADVERSE REACTIONS/*Postmarketing Experience*** section has been changed from:

   The following adverse reaction has been reported in postmarketing experience: Reports of aplastic anemia have been rare and received only when carvedilol was administered concomitantly with other medications associated with the event.

To:

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. Urinary incontinence in women (which resolved upon discontinuation of the medication) and interstitial pneumonitis have been reported rarely.

We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling package insert submitted June 29, 2005.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that the labeling be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper.

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, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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:

Ms. Melissa Robb
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

{See appended electronic signature page}

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

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

/s/

Norman Stockbridge

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