

1001 G Street, N.W.  
Suite 500 West  
Washington, D.C. 20001  
tel. 202.434.4100  
fax 202.434.4646

1005 7 1120 1040

March 16, 2007

Writer's Direct Access  
**Frederick A. Stearns**  
(202) 434-4288  
stearns@khlaw.com

**Via FedEx**

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Re: ANDA Suitability Petition: Carvedilol Phosphate Extended-Release Tablets**

The undersigned hereby submits, in quadruplicate, this Suitability Petition pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(j)(2)(C), and the Food and Drug Administration's (FDA's) regulations 21 C.F.R. §§ 314.93, 10.25 and 10.30.

**A. Action Requested**

This Suitability Petition requests a declaration by the Commissioner of Food and Drugs that an Abbreviated New Drug Application ("ANDA") may be filed for the drug carvedilol phosphate in an extended-release tablet dosage form.

**B. Statement of Grounds**

An ANDA may be filed for the approval of a new drug that is the same as a reference listed drug ("RLD"). 21 U.S.C. § 355(j)(2)(A). An ANDA may also be filed for a new drug, which is the same as an RLD except for a difference in dosage form, provided that FDA has granted permission to file such an ANDA upon the submission and approval of a pertinent "suitability" petition. 21 U.S.C. § 355(j)(2)(C); 21 C.F.R. § 314.93(b). FDA is authorized to approve a suitability petition seeking a change in dosage form from an RLD. *Id.*

The specific RLD upon which this Petition is based is Coreg CR (carvedilol phosphate) Extended-Release Capsules, a prescription drug that is indicated in its FDA-approved labeling for the treatment of essential hypertension and congestive heart failure (CHF) (See Attachments 1 and 2 hereto). The approved NDA for the RLD (#022-012) is held by GlaxoSmithKline. *Id.*

The proposed drug product will contain the same active ingredient as the RLD (carvedilol phosphate), and will have the same strengths (10 mg, 20 mg, 40 mg & 80 mg) and the same route of administration (oral) as the RLD. The proposed drug product will differ from the RLD only in its dosage form – a tablet rather than a capsule. The labeling of the proposed drug product will also be the same as the currently approved labeling for the RLD, except for changes that are

2007P-0103

CPI

## KELLER AND HECKMAN LLP

Division of Dockets Management (HFA-305)

March 16, 2007

Page 2

required because of the difference in manufacturer, and the difference in dosage form proposed under this Petition (see Attachment 3).

FDA has previously approved an ANDA suitability petition allowing a change in dosage form from a delayed-release capsule to a delayed-release tablet (see Attachment 4).

### Pediatric Assessment Waiver Request

Pursuant to the Pediatric Research Equity Act of 2003 ("PREA"), 21 U.S.C. § 355B(a)(4)(ii), a full waiver of the requirement to submit an assessment of carvedilol phosphate in an extended-release tablet dosage form in a pediatric population is requested, on the grounds that:

- (1) There is evidence suggesting that carvedilol would be ineffective in pediatric age groups with CHF. In a double-blind trial, 161 children (mean age 6 years, range 2 months to 17 years; 45% less than 2 years old) with chronic heart failure {NYHA class II-IV, left ventricular ejection fraction <40% for children with a systemic left ventricle (LV), and moderate-severe ventricular dysfunction qualitatively by echo for those with a systemic ventricle that was not an LV} who were receiving standard background treatment were randomized to placebo or to two dose levels of carvedilol. These dose levels produced placebo-corrected heart rate reduction of 4-6 heart beats per minute, indicative of beta-blockade activity. Exposure appeared to be lower in pediatric subjects than adults. After 8 months of follow-up, there was no significant effect of treatment on clinical outcomes (see Attachment 5).
- (2) This pharmaceutical alternative drug product does not represent a meaningful therapeutic benefit over existing therapies for hypertension in pediatric patients and is not likely to be used in a substantial number of pediatric patients. According to FDA approved labeling the antihypertensive effectiveness of the following drugs has been established in pediatric patients ages 6 to 16 years: amlodipine, benazepril, lisinopril and losartan. The Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents (NHLBI Guideline, May 2005) provides dosing recommendations for many other available antihypertensive drugs used in the management of hypertension in children 1-17 years old (see Attachment 6).

### **C. Environmental Impact**

Petitioner claims a categorical exclusion from the requirement of an environmental assessment or environmental impact statement pursuant to 21 C.F.R. § 25.31.

## KELLER AND HECKMAN LLP

Division of Dockets Management (HFA-305)  
March 16, 2007  
Page 3

### **D. Economic Impact**

Pursuant to 21 C.F.R. § 10.30 (b), economic impact information is to be submitted only when requested by the Commissioner following review of this Petition.

### **E. Certification**

The undersigned certifies that, to their best knowledge and belief, this Suitability Petition includes all information and views upon which the Petition relies, and includes representative data and information known to Petitioner that are unfavorable to the Petition.

Respectfully submitted,



Frederick A. Stearns

cc: Gary J. Buehler (Director, Office of Generic Drugs) (with attachments)

#### Attachments:

1. Approved Drug Products with Therapeutic Equivalence Evaluations ("The Electronic Orange Book"). Coreg CR (carvedilol phosphate) Extended-Release Capsules
2. Approved labeling for Coreg CR
3. Proposed labeling for Carvedilol Extended-Release Tablets
4. FDA response to Docket 99P-1087/CP1
5. Medical/Clinical Pharmacology Review of NDA 20-297/S-022 (from FDA website "Summaries of Medical and Clinical Pharmacology Reviews of Pediatric Studies")
6. Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents (May, 2005)