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RESEARCH**

*APPLICATION NUMBER:*

**22-021**

**PHARMACOLOGY REVIEW**

NDA 22-021

**PHARMACOLOGY REVIEW OF ORIGINAL 505(B)(2) APPLICATION**

**SUBMISSION DATE:** 10 January 2006

**CENTER RECEIPT DATE:** 12 January 2006

**REVIEW COMPLETION DATE:** 05 May 2006

**REVIEWER:** C.A. Resnick, Ph.D.

Supervisory Pharmacologist

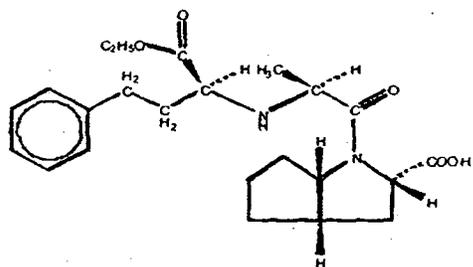
Division of Cardiovascular & Renal Products

**SPONSOR:** Cobalt Pharmaceuticals Inc.

**DRUG PRODUCT:** Ramipril Tablets

**REFERENCED LISTED DRUG PRODUCT:** Altace® capsules (King Pharmaceuticals)

**DRUG SUBSTANCE:** ramipril



Molecular Formula:  $C_{23}H_{32}N_2O_5$

Molecular Weight: 416.5

CAS No. 87333-19-5

Pharmacologic Category: angiotensin-converting enzyme inhibitor

**PROPOSED INDICATION:** hypertension

**FORMULATION AND PROPOSED ROUTE OF ADMINISTRATION:** Tablets for oral administration contain 1.25 mg, 2.5 mg, 5 mg or 10 mg of ramipril plus the following inactive ingredients: calcium sulphate dehydrate, pregelatinized starch, sodium bicarbonate and sodium stearyl fumarate.

**PROPOSED DOSAGE REGIMEN:** The recommended initial dose for patients not receiving a diuretic is 2.5 mg once a day; for those on a diuretic, 1.25 mg once a day. The usual maintenance dosage range is 2.5 to 20 mg per day administered as a single dose or in two equally divided doses. For patients with both hypertension and renal impairment, the recommended initial dose is 1.25 mg once a day with titration up to a maximum daily dose of 5 mg.

**NONCLINICAL PHARMACOLOGY/TOXICOLOGY DATA:** None. The application relies on the prior approval of King Pharmaceutical's Altace®tablets (NDA 19-901).

**PROPOSED LABELING:** Essentially identical to the labeling for the referenced product, King Pharmaceutical's Altace® Tablets. There are no differences between the package inserts in those subsections that deal with the results of nonclinical studies.

**EVALUATION:** This 505(b)(2) application for ramipril tablets relies on the prior approval of King Pharmaceuticals' NDA 19-901 for Altace (ramipril) Tablets in lieu of providing non-clinical safety data. There are no differences between the two products in terms of proposed usage and the prior Agency findings of safety and efficacy for the King Pharmaceuticals product serve as an acceptable substitute for toxicology studies of the Cobalt product.

**RECOMMENDATION:** The application is approvable from the perspective of pharmacology.

*NDA 22021.doc*  
*9 May 2006*

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/s/

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Charles Resnick  
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PHARMACOLOGIST