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RESEARCH**

APPLICATION NUMBER:

22-026

PHARMACOLOGY REVIEW(S)

NDA 22-026

PHARMACOLOGY REVIEW OF ORIGINAL 505(b)(2) APPLICATION

SUBMISSION DATE: 31 January 2006

CENTER RECEIPT DATE: 01 February 2006

REVIEW COMPLETION DATE: 08 May 2006

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

Supervisory Pharmacologist

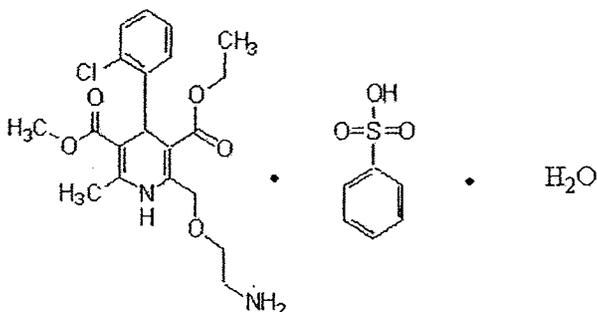
Division of Cardiovascular & Renal Products

SPONSOR: Synthon Pharmaceuticals Inc.

DRUG PRODUCT: Amlodipine Besylate Orally Disintegrating Tablets

REFERENCED LISTED DRUG PRODUCT: Norvasc® Tablets (Pfizer Inc.) NDA 19-787

DRUG SUBSTANCE: amlodipine besylate monohydrate



Molecular Formula: C₂₀H₂₅ClN₂O₅•C₆H₆SO₃•H₂O

Molecular Weight: 585.07

CAS No. 111470-99-6

Pharmacologic Category: calcium channel blocker

PROPOSED INDICATIONS: hypertension, chronic stable angina and vasospastic angina

FORMULATION AND PROPOSED ROUTE OF ADMINISTRATION: Orally disintegrating tablet (ODT) containing 2.5, 5 or 10 mg of amlodipine (supplied as amlodipine besylate) plus the following inactive ingredients: hydroxypropyl cellulose, iron oxide red (10 mg tablets only), iron oxide yellow (5 mg tablets only), magnesium stearate, mint menthol, microcrystalline cellulose and sucralose.

PROPOSED DOSAGE REGIMEN: Initial adult dosage of 2.5 to 10 mg once daily, depending on indication, size and age of the patient and the presence or absence of hepatic insufficiency (patients other than small, fragile or elderly, or those with hepatic insufficiency usually started on

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5 mg once daily, 10 mg once daily for angina patients. The effective antihypertensive oral dose in pediatric patients (ages 6-17) is 2.5 to 5 mg once daily.

NONCLINICAL PHARMACOLOGY/TOXICOLOGY DATA: None. The application relies on the prior approval of Pfizer's Norvasc® Tablets.

PROPOSED LABELING: Other than changes dictated by the new formulation, the labeling is essentially identical to the labeling for the referenced product, Pfizer's Norvasc® Tablets. There are no differences between the two package inserts in those subsections that deal with the results of nonclinical safety studies.

EVALUATION: This 505(b)(2) application for amlodipine besylate orally disintegrating tablets relies on the prior approval of Pfizer's NDA 19787 for Norvasc® (amlodipine besylate) tablets in lieu of providing non-clinical safety data. There are no differences between the two products in terms of proposed usage (i.e., indications, dosage and route of administration) and the prior Agency findings of safety and efficacy for the Pfizer product serve as an acceptable substitute for toxicology studies of the Synthon product.

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

*NDA 22026
9 May 2006*