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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-392

Pharmacology Review(s)

NDA 21-392 **Diltiazem HCl Extended Release Tablets**

PHARMACOLOGY REVIEW OF ORIGINAL APPLICATION

SUBMISION DATE: 08 June 2001
CENTER RECEIPT DATE: 11 June 2001
REVIEW COMPLETION DATE: 09 August 2001

SPONSOR: Biovail Laboratories Inc.

AGENT: John Dubeck
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Washington D.C.
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REVIEWER: C.A. Resnick, Ph.D.
Supervisory Pharmacologist
Division of CardioRenal Drug Products (HFD-110)

ACTIVE INGREDIENT: **diltiazem** HCl, a calcium channel blocker

FORMULATION: 240, 300 or 360 mg diltiazem HCl in an extended release tablet intended for once daily administration. Excipients include carnauba wax NF, colloidal silicon dioxide NF, croscarmellose sodium NF, polyacrylate dispersion 30% (Eudragit NE 30 D), hydrogenated vegetable oil NF, hydroxypropylmethylcellulose USP, magnesium stearate NF, microcrystalline cellulose NF, microcrystalline wax NF, [ ] pregelatinized starch NF, polysorbate NF, povidone USP, simethicone USP, sucrose stearate, talc USP and titanium dioxide USP. The [ ] carnauba wax are components of the tablet coating. The other ingredients are components of the drug-coated beads. The formulation was designed to be bioequivalent to Biovail's approved once-daily Diltiazem HCl extended release capsule (NDA 20-939).

PROPOSED INDICATION: Hypertension

PROPOSED DOSAGE REGIMEN: Proposed labeling states that, "when used as monotherapy, reasonable starting doses are 180 to 240 mg once daily, although some patients may respond to lower doses." It also notes that [ ] and that "doses to 540 mg have been studied in clinical trials."

NONCLINCIAL PHARMACOLOGY/TOXICOLOGY DATA: None included. Sponsor claims right of reference to Cardizem CD NDA 20-062 and Cardizem Tablet NDA 18-602. (Letter of authorization from Aventis Pharmaceuticals included in submission.)

LABELING: Statements regarding animal and *in vitro* studies are the same as in the approved labeling for Biovail's Diltiazem HCl Extended Release Capsule (NDA 20-939).

EVALUATION: This NDA is for a tablet formulation of the sponsor's approved extended release capsule formulation of diltiazem HCl. The new formulation is claimed to be bioequivalent to the marketed product. The only non-compendial ingredients in the new (tablet) product (sucrose stearate and Eudragit NE30D) are also ingredients of the marketed product. As there are no differences between the sponsor's tablet product and the sponsor's approved capsule product in the way they are used (same doses and same indication), the basis for approval of the currently marketed product is also the basis for approval of the product that is the subject of this review.

RECOMMENDATION: Approvable

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/s/

Charles Resnick
8/9/01 06:24:22 PM
PHARMACOLOGIST