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Application Number 21-472

PHARMACOLOGY REVIEW(S)

Pharmacology /Toxicology Cover Sheet

NDA number: 21472

Review number: No.1

Sequence number/date/type of submission: Original submission/Dec. 18, 2001

Information to sponsor: Yes No

Sponsor and/or agent: Banner Pharmacaps Inc.

Manufacturer for drug substance:

Reviewer name: Conrad H. Chen, Ph.D.

Division name: Anti-inflammatory, Analgesic, and Ophthalmic Drug Products

HFD#: 550

Review completion date: September 5, 2002

Drug: 200mg Ibuprofen Capsules (Softgels)

Relevant INDs/NDAs/DMFs: I-62553, ANDA-74782, N-20402, N-19012, and N-17463.

Drug class: NSAID

Indication: for OTC use, 1

Clinical formulation: A soft gelatin capsule of Ibuprofen free acid solubilized in a mixture of PEG, Povidone, and Vitamin E Polyethylene Glycol Succinate (TPGS).

(Each 200 ibuprofen capsule contains 200mg ibuprofen, PEG, povidone, and TPGS. The total fill amount of a capsule is The total weight of a capsule including the fill amount and the capsule shell is

Route of administration: Oral.

Proposed use: OTC.

Proposed dose: , not to exceed 6 softgels in 24 hours.

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Pharmacology/Toxicology Review

Non-clinical Pharmacology, Toxicology and Pharmacokinetics.

This application cross-references to the followings for the non-clinical information:

Approved NDA 17463 (Upjohn, Motrin IB Gelcap, Ibuprofen Tablets).

Approved NDA 18989 (Whitehall-Robbins, Advil, Ibuprofen Tablets).

Approved NDA 20402 (Sandoz, Provel, Ibuprofen Softgels, marketed by Whitehall-Robbins as Advil Liqui-Gels).

Approved ANDA 74782 (Pharmaceutical Formulations, Inc, Ibuprofen Capsules).

Detailed Conclusions and Recommendations.

Ibuprofen use was approved in 1974 for prescription use and in 1984 for OTC use. The drug product of this NDA is 200mg ibuprofen soft gelatin capsules filled with liquid ibuprofen free acid. Ibuprofen free acid is solubilized with Polyethylene glycol (PEG) ← Povidone, and Vitamin E Polyethylene Glycol Succinate. The inactive ingredients in the formulation are all compendium products commonly used in the pharmaceutical products.

In the approved NDA 20402, Ibuprofen free acid was also solubilized with PEG ← During the shelf life it was anticipated that some amount of _____ would be formed in the capsule.

Based on the maximum clinical dose of 6 capsules a day, the maximum daily ingestion of _____ would be _____). This dose amounts to _____ in a 60kg body weight person. Since no toxic effects were found in 14-day and 4-day rat studies at 100mg/kg/day, the daily ingestion of _____ in humans probably is safe.

Based on the information available in the literature and those cited by the sponsor, the reviewing pharmacologist recommends the approval of NDA 21472.

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this page is the manifestation of the electronic signature.**

/s/

Conrad Chen

9/16/02 02:13:23 PM

PHARMACOLOGIST

The NDA is recommended for approval based on the
information from literature.

The hard copy of review has been signed.

Josie Yang

9/16/02 02:46:36 PM

PHARMACOLOGIST

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