CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number NDA 21-082

PHARMACOLOGY REVIEW(S)

Hilfiker

DIVISION OF PULMONARY AND ALLERGY DRUG PRODUCTS FEB - 1 2000
REVIEW AND EVALUATION OF PHARMACOLOGY AND TOXICOLOGY DATA
Original Submission: Review #1

NDA 21-082

Reviewer: Misoon Y. Chun, Pharm.D., DABT
Date of Submission: October 7, 1999
Date of Review: January 28, 2000

Information to be Conveyed to Sonsor: Yes ( ), No (x)

Sponsor: Novartis Consumer Health, Inc. (NCH)
560 Morris Avenue
Summit, NJ 07901-1312
Tel: 908-273-7600
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Drug Name: Tavist® Allergy/Sinus/Headache Tablets
(Clemastine fumarate/Acetaminophen/Pseudoephedrine hydrochloride, 0.335/500/30 mg Tablet)

Indication:

- Temporary relief of sneezing, runny nose, and itching of the nose or throat, and itchy watery eyes due to hay fever (allergic rhinitis), and sneezing and runny nose due to the common cold.
- Temporary relief of nasal and sinus congestion due to the common cold, hay fever, or other upper respiratory allergies, or ———
- Temporary relief of minor aches, pains, headache, ——— , and fever associated with the common cold; temporary relief of minor aches, pains and headache associated with hay fever, allergic rhinitis, and ———

Proposed Dose: For adults and children 12 years of age and older is 2 caplets every 6 hours as needed, and not more than 8 caplets in 24 hours unless directed by a doctor.

Related INDs/NDAs:

IND ———
IND — (Clemastine fumarate/Acetaminophen/Pseudoephedrine hydrochloride (0.335/500/30 mg per tablet)
NDA 17-661 (Tavist®, 2.68 mg tablet) Rx
NDA 18-675 (Tavist® syrup) Rx
NDA 18-298 (Tavist-D® tablet) OTC
NDA 20-925 (Tavist-1®, 1.34 mg tablet) OTC
NDA 20-640 (Tavist-D® ———) OTC

Background:

At the pre-NDA meeting held on December 9, 1996, it was determined that only two primary issues were to be addressed in the NDA. Because pseudoephedrine hydrochloride (PSE) and acetaminophen (APAP) are approved OTC drug monograph ingredients, it was only necessary to demonstrate the absence of a pharmacokinetic interaction among the components, and then to demonstrate that the revised dose schedule for clemastine (0.5 mg q6h) was effective and had a safety profile comparable to that of clemastine at the approved OTC dose (1 mg q 12h).

Evaluation and Recommendation:

There were no new preclinical pharmacology or toxicology studies conducted in support of this application. Preclinical information on clemastine was referenced to NDA 17-661 which was approved on February 25, 1977.

The drug substances formulated into the new antihistamine/decongestant/analgesic combination drug product are not new chemical entities. Each of the active ingredients has an extensive history of safe over-the counter use. The individual and total daily dose levels for pseudoephedrine hydrochloride (60 mg — 6h) and acetaminophen (1000 mg q6h) in the new product are the same as doses already approved in existing nonprescription products. Clemastine is not an antihistamine listed in the OTC Monograph; therefore, the comparability of the proposed dose schedule for clemastine (0.5 mg q6h) to that of clemastine at the approved OTC dose (1 mg q 12h) was studied for this NDA. There are no safety concerns for the drug substances used in this formulation from preclinical standpoint.

If the proposed issues discussed at the pre-NDA meeting have been adequately addressed from the clinical point of view, this NDA is approvable from the standpoint of pharmacology/toxicology.

APPEARS THIS WAY
ON ORIGINAL

/S/ Feb 1, 2000
Misoon Y. Chun, Pharm.D., D.A.B.T.
Pharmacologist/Toxicologist

NDA 21-082
cc: HFD-570/Division File
HFD-570/Lee/Medical Reviewer
HFD-570/Hilfiker/PM
HFD-570/Chun/Pharm/Tox Reviewer
HFD-570/Huff/Pharm/Tox Team Leader

/S/ 2-1-00