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APPLICATION NUMBER: 20802

PHARMACOLOGY REVIEW(S)

COOK

FEB 26 1997

Pharmacology Review

NDA 20-802

Sponsor: Bristol Myers Products

Date Submitted: Jan 14, 1997

Date received by CDR: Jan 15, 1997

Date Assigned: Jan 28, 1997

Date of Review: Feb 19, 1997

Drug: Excedrin Extra Strength Tablet

Category: OTC Analgesic

Indication: Temporary relief of migraine headache

APPEARS THIS WAY
ON ORIGINAL

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The sponsor has submitted the NDA on Excedrin Extra Strength tablets, caplets and geltabs for the temporary relief of migraine pain as an OTC product. Each formulation will contain acetaminophen 250 mg, aspirin 250 mg and caffeine 65 mg. A similar formulation has been marketed as OTC analgesic for the temporary relief of headache, sinusitis, cold, muscular ache, menstrual discomfort, toothache and minor arthritis pain. For the inclusion of migraine pain as an indication, the sponsor has conducted safety and efficacy trials. The daily maximum recommended dose is 8 tablets, caplets or geltabs for adults. The product is not recommended for children below 12 years of age.

The sponsor submitted several literature references on the pharmacodynamic, pharmacokinetic and toxicity of the combination. These data were reviewed for IND on April 17, 1995. However, no additional study recommendation was made during the IND review except monitoring the plasma levels of analgesics in the target population. The acute toxicity of the formulation were examined in mice. The toxic signs were tremor and ataxia. The literature report showed that the long term chronic dosing of the analgesic combination showed papillary necrosis in the kidney. Several warnings have been recommended for the draft package label for the OTC uses. From the preclinical safety point of view, the product is approvable for the temporary relief of migraine headache as an OTC medication.

Recommendation: Preclinical safety point of view the product is approvable for the temporary relief of migraine headache.



Asoke Mukherjee
Pharmacologist

cc: Orig NDA #20,802
HFD-550/Div File
HFD-550/Reviewer
HFD-550/CSO
HFD-345
R/D Init. by:
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Concurred by Conrad H. Chen 2-26-97