CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-586

PHARMACOLOGY REVIEW

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Pharm/Tox Review

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EXECUTIVE SUMMARY

1. Recommendations

1.1 Recommendation on approvability: There are no outstanding preclinical issues and the NDA is approvable from a pharmacology/toxicology perspective.

1.2 Recommendation for nonclinical studies: None

1.3 Recommendations on labeling: None as the labels for topical skin disinfectants use an OTC drug label format and do not contain sections reviewed by a pharmacologist that are usually found in prescription drug labels.

2. Summary of nonclinical findings

2.1 Brief overview of nonclinical findings: Very few studies were performed to support this NDA as the individual components have been in clinical use for a long time and the DuraPrep™ product has been marketed since 1988. The genetic toxicology studies that were performed (mouse lymphoma and chromosomal aberrations in CHO cells) were negative. The skin sensitization assay in guinea pigs did not show sensitization potential.

2.2 Pharmacologic activity: Not applicable

2.3 Nonclinical safety issues relevant to clinical use: Iodine is available in the U.S. for topical use at 2% iodine and 2.4% sodium iodide, 2% tincture of iodine and 2.4% sodium iodide with 47% alcohol. Additional formulations include iodine ointments, iodine ointments with salicylic acid, Lugol's solution, potassium iodide, strong tincture of iodine (7% solution) and many others. Isopropyl alcohol (70%) as well as ethanol (80%) and n-propanol (50%) have been used for disinfection of skin for many years. Isopropyl alcohol is also used in cosmetics and perfumes, as a solvent and as a vehicle for germicidal compounds. These products have been used for many years and the safety profile of the ingredients is well-characterized.

3.2 PHARMACOLOGY

3.2.1 Brief summary: No studies submitted

3.2.2 Primary pharmacodynamics: No studies submitted

3.2.3 Secondary pharmacodynamics: No studies submitted

3.2.4 Safety pharmacology: No studies submitted

3.2.5 Pharmacodynamic drug interactions : No studies submitted

3.3 PHARMACOKINETICS/TOXICOKINETICS

3.3.1 Brief summary: No studies submitted

3.4 TOXICOLOGY

3.4.1 Overall toxicology summary

General toxicology: Dermal sensitization study (see IND review 10/25/00) in guinea pigs did not demonstrate skin sensitization.

Genetic toxicology: See IND review 5/27/97. DuraPrep™ was negative in the mouse lymphoma assay and chromosomal aberration assay in CHO cells.

Carcinogenicity: No studies were performed for this NDA.

Reproductive toxicology: No studies were performed for this NDA.

Special toxicology: No studies were performed for this NDA.

3.4.2 Single-dose toxicity: No studies were performed for this NDA.

3.4.3 Repeat-dose toxicity: No studies were performed for this NDA.

3.4.4. Genetic toxicology
The mouse lymphoma assay and the chromosomal aberration assay in CHO cells were performed and were negative. See IND review for details.

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/s/

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