CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-780

PHARMACOLOGY REVIEW

HFD-520 / Duvall Mills

MAY 15 2000

REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA
Division of Anti-infective Drug Products, HFD-520

NDA number: 50-780 (000)

KEY WORDS: Duplex, cefuroxime

Reviewer Name: Kenneth Seethaler, R.Ph., Ph.D., D.A.B.T.

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Submission format: Paper NDA

Scientific literature reviewed: Yes ( ) No (x)

Information to sponsor: Yes (x) No ( )

Sponsor: B. Braun Medical Inc.
2525 McGaw Avenue
Irvine, CA 92623

Contact person: John D'Angelo
Vice President, Regulatory and Medical Affairs
Phone 949-660-2517

Drug: Cefuroxime for Injection in Duplex container

INTRODUCTION

This NDA seeks approval to market cefuroxime and dextrose injection USP, in a "Duplex" container. The Duplex container is a flexible plastic, dual chamber drug delivery system, designed for intravenous injection only. The contents of the drug chamber and diluent chamber remain separated until pressure is applied to the diluent chamber, to break the seal between the two chambers, and cause mixing of the drug and diluent. After mixing, the application of additional pressure breaks a second seal, and allows the reconstituted solution to flow into the set port. The safety of the Duplex container has been demonstrated by the results of USP compendial testing for extractables.

Cefuroxime is an approved product that has been marketed in the United States for many years. This sponsor seeks to rely on data from clinical studies on the innovator product, Zinacef (Glaxo-Wellcome).

RECOMMENDATIONS

From the Pharmacology/Toxicology perspective, there is no objection to the approval of this NDA, since cefuroxime has already been approved by FDA. However, the sponsor's proposed labeling is not in the latest format, and the sponsor should be requested to address the following comments pertaining to the **PRECAUTIONS** section of the label.

In the **Carcinogenesis, Mutagenesis, Impairment of Fertility** section, the sentence now reads: "Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests." (the particular laboratory tests used, should be identified).

The next sentence now reads: "Reproductive studies revealed no impairment of fertility in animals." (the species of animals and the studies performed, should be identified).

In the **Pregnancy: Teratogenic Effects: Pregnancy Category B:** section, the sentence now reads: "Reproduction studies have been performed in mice and rabbits at doses up to 60 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime." (the multiple of the human dose should be given separately for mice and rabbits, the dosage units should be presented, and the basis for the comparison between the human dose and the animal doses should be given, and if it is mg/kg, it should be converted to either mg/m^2 or AUCs).

/S/

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cc: Original NDA 50-780
HFD-104
HFD-340
HFD-520
HFD-520/Pharm/K. Seethaler
HFD-520/MO/J.Alexander
HFD-520/Micro/S.Altaie
HFD-520/Chem/S.Pagay
HFD-520/CSO/B.Duval-Miller
HFD-520/Biopharm/F.Pelsor
HFD-520/Biostat/T.Lin

Concurrence only:

HFD-520/R. Osterberg /S/ 5/15/00

HFD-520/L. Gavrilovich 5/15/00