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RESEARCH**

APPLICATION NUMBER:

50-779

PHARMACOLOGY REVIEW

OCT 15 1999

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

NDA number: 50-779 (000)

KEY WORDS: Duplex, cefazolin

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

Date of submission: August 23, 1999

Review completion date: October 8, 1999

Submission format: Paper NDA (no clinical or preclinical study reports)

Scientific literature reviewed: Yes () No (x)

Information to sponsor: Yes (x) No ()

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

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

Drug: Cefazolin for Injection in Duplex container

INTRODUCTION

This NDA seeks approval to market cefazolin 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.

Cefazolin 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, Ancef (SmithKline Beecham). Braun Medical claims that the applicable patents are either expired, or are not infringed.

RECOMMENDATIONS

From the Pharmacology/Toxicology perspective, there is no objection to the approval of this NDA, assuming the absence of patent infringements, and assuming the safe operation of the Duplex delivery system.

The sponsor's proposed labeling has been modified from the Physicians Desk Reference for Ancef, but the labeling is not in the latest format. For example, the basis for the comparison between the doses in animal reproduction studies, and the human dose is not stated. This comparison should be made on the basis of either AUCs or milligrams per square meter.

Also, the statement that mutagenicity and carcinogenicity studies have not been performed, may no longer be true, and should be confirmed.

It is recommended that the PRECAUTIONS section of the label be revised to correct these shortcomings.

IS/

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cc: Original NDA 50-779
HFD-104
HFD-340
HFD-520
HFD-520/Pharm/K. Seethaler
HFD-520/MO/J.Alexander
HFD-520/Micro/F.Marsik
HFD-520/Chem/A.Yu
HFD-520/CSO/B.Duval-Miller

Concurrence only:

HFD-520/R. Osterberg IS/10/15/99
HFD-520/L. Gavrilovich IS/10/12/99