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APPLICATION NUMBER: **20-574**

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

CLINICAL PHARMACOLOGY/BIOPHARMACEUTICS REVIEW

NDA: 20-574

SUBMISSION DATE: November 25, 1997

Clotrimazole Vaginal Cream, 2%
Gynae-Lotrimin 3™

REVIEWER: Funmilayo Ajayi, Ph.D.

Schering Plough
110 Allen Road, Liberty Corner
New Jersey 07938

TYPE OF SUBMISSION: Original NDA

Background: This submission is for a 3-day treatment of vaginal candidiasis.

Findings: The review for this product was completed by Dr. Ette in August 1995. Thus, no further review is indicated at this time.

Recommendation: I concur with the previous recommendation by Dr. Ette.

/S/ 4/16/98
Funmilayo O. Ajayi, Ph.D.
Div. of Pharmaceutical Evaluation III

cc: NDA 20-574, HFD-590 (Clinical Division)
HFD-880 (DPE3, Ajayi)
CDR (B. Murphy)

AUG 3 1995

NDA 20-574

Clotrimazole Vaginal Cream
(Gyne-Lotrimin 3™)

SUBMISSION DATE: 04-27-95

Schering Plough
110 Allen Road
P.O. Box 276
Liberty Corner
New Jersey 07938-0276

REVIEWER: Ene Ette, Ph.D

BIOPHARMACEUTICS REVIEW

BACKGROUND:

This is an NDA filed for Gyne-Lotrimin 3™ 3-Day Vaginal Cream, a 2% clotrimazole antifungal cream for over-the-counter (OTC) use. It is to be administered once daily, preferably at bedtime.

3 - 10% of clotrimazole (a synthetic antifungal agent) is absorbed from the vagina, while < 0.5% is absorbed from the intact skin. Fungicidal concentration remain for as long as 3 days after application of the drug. The small amount absorbed is metabolized in the liver and excreted in the bile.

SYNOPSIS:

The Sponsor has cited an agreement reached in a meeting held with representatives of HFD-520 and the Office of OTC Drug Evaluation on March 10, 1992 that no pharmacokinetic and/or bioavailability studies would be required.

The Sponsor also stated that agreement was reached for a dose-ranging study with 1%, 2%, and 4% clotrimazole cream administered for 3 consecutive days and 1% clotrimazole cream administered for 7 days should be conducted. This was to be followed by two adequate well controlled efficacy studies to compare the selected 3-day dose with the OTC approved dose of 1% clotrimazole vaginal cream for 7 consecutive days.

In addition, the Sponsor stated:

"The same inactive ingredients are used in the 1% vaginal cream for either 3-day or 7-day use and in the 2% and 4% vaginal creams."

"At the March 10, 1992 meeting, the FDA requested that the selected 3-day therapy be compared with the "gold-standard" therapy of 1% clotrimazole cream for 7 consecutive days as an adequate basis for demonstrating efficacy."

COMMENT:

No specific mention was made of any pharmacokinetic studies in meeting minutes (see the last page of the minutes of the FDA / Sponsor meeting). However, the Sponsor was advised to carry out two well controlled clinical trials to demonstrate clinical equivalence between the 2% cream 3-day therapy versus the 7 therapy with the 1% cream.