CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-980

BIOEQUIVALENCE REVIEW(S)

JUN 15 1998

Terbinafine HCl Cream 1%
NDA 20-980
Lamisil® Cream 1%
Reviewer: E.D. Bashaw, Pharm.D.
APW

Novartis Pharmaceuticals
East Hanover, NJ 07936

Submission Date:
March 30, 1998

Review of an Rx to OTC Switch

Background

Terbinafine is a broad spectrum antifungal agent belonging to the allylamine family. It exerts its antifungal activity through inhibition of fungal biosynthesis of ergosterol at the point of squalene epoxidation. Cell death follows the disruption of cell membranes and the interruption of cell wall synthesis. Currently terbinafine is available as a prescription only product on the U.S. market as an oral 250mg tablet (NDA 20-539), as a 1% topical cream (NDA 20-192), and as a 1% topical spray (NDA 20-749). This NDA is to allow for the OTC switch of the 1% Cream formulation for interdigital tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm). Prescription marketing will be retained for the indication of plantar tinea pedis (moccasin type).

Formulation

The formulation of the OTC product is identical to that of the currently marketed prescription product. In the original NDA review dated 12/11/92 a qualitative formulation of the product was included in the review. The following paragraph was excerpted from the original NDA review:

In this submission the sponsor supplies no new chemistry information beyond a reference back to the original NDA submission materials for the specifications and manufacturing controls section.

Biopharmaceutics

Lamisil® Cream 1% was originally reviewed in the Division of Biopharmaceutics by Emil Samara, Ph.D. in 1992 (approvable) and by Jennifer Keifer, Ph.D. (approved) in 1994. In the original NDA review the sponsor submitted the results of four in vivo pharmacokinetic studies:

1. A radiolabeled study in normal volunteers

2. A single and multiple dose (BID) study of the topical absorption of 1gm of 1% terbinafine cream in individuals with compromised skin.
3. A single and multiple dose (BID) study of the topical absorption of 1% terbinafine cream in patients with tinea cruris.
4. A single and multiple dose (BID) study of the topical absorption of 1% terbinafine cream in patients with pityriasis versicolor (aka: tinea versicolor).

Review of these studies found that terbinafine was minimally absorbed in both patients and normal volunteers with peak levels usually being <15ng/ml. There were no biopharmaceutic deficiencies beyond a request for additional analytical information which was subsequently submitted and reviewed in 1994.

One potential concern for this product would be a potential for extension of the product in to subjects who have not been adequately studied. While pediatric patients were not included in the original biopharmaceutic portion of the NDA, the current Rx label allows use down to an age of 12 yrs. As the proposed OTC label includes language prohibiting the use of the product in children under the age of 12 yrs. there does not appear to be a problem related to an extension of use in this population.

Labeling

Attached is a copy of the proposed package insert/patient leaflet. It contains no biopharmaceutic information beyond the aforementioned prohibition on use in children under 12 yrs.

Recommendation

This application for OTC marketing represents a partial move of a product from prescription to OTC status. As the population to be treated is identical to that which was originally studied with the prescription product and as there are no outstanding biopharmaceutic commitments from the 1% cream approval, the marketing of this product is acceptable from a biopharmaceutic perspective.

/S/ 6/10/98

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Secondary Review, John Lazor, Pharm.D. /S/ 6/15/98
For John Lazor

CC: NDA 20-980 (ORIG),
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