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DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

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DATE: MAR 30 2005

FROM: Director  
Division of OTC Drug Products, HFD-560

SUBJECT: Material for Docket No. 2004P-0490/CPI

TO: Dockets Management Branch, HFA-305

The attached material should be placed on public display under the above referenced Docket No.

This material should be cross-referenced to Comment No. CPI

  
Charles J. Ganley, M.D.

Attachment



MAR 30 2005

Francis W. Busch  
Executive Vice President  
Research and Development  
ProStrong Inc.  
20 Main Street  
Oakville, CT 06779

Re: Docket No. 2004P-0490  
Comment No. CP1

Dear Mr. Busch:

This letter is in response to your citizen petition dated October 27, 2004, on over-the-counter (OTC) topical antifungal drug products. Your petition was filed as CP1 under Docket No. 2004P-0490 in the Division of Dockets Management.

In your petition, you request that the Commissioner of the Food and Drug Administration (FDA) amend the monograph for topical antifungal drug products (21 CFR part 333 subpart C) to allow the use of 1% tolnaftate for the prevention of fungal infections of the nail or the prevention of dermatophytes of the nail. Currently, under §§ 333.210(e) and 333.250(b)(1), 1% tolnaftate is generally recognized as safe and effective (GRASE) for the treatment of athlete's foot, jock itch, and ringworm. Tolnaftate (1%) is also the only GRASE active ingredient for the prevention of athlete's foot (§ 333.250(b)(2)). The prevention of nail fungal infections is not currently a GRASE indication for any topical antifungal active ingredient. Any topical antifungal product labeled for use on the nails is nonmonograph (*i.e.*, not GRASE) under 21 CFR 310.545(a)(22)(iii). Accordingly, § 333.250(d)(1) requires OTC topical antifungal drug products labeled as treating athlete's foot, jock itch, and ringworm to include the statement "This product is not effective on the scalp or nails."

To support your request, you state that prevention of nail fungal infections is a major consumer concern because, once infected, treatment is extremely difficult and limited to prescription drugs. You contend that the effectiveness of tolnaftate in preventing nail fungal infections is supported by its recognition as GRASE in the prevention of athlete's foot. You make two points concerning the safety of tolnaftate in preventing nail fungal infections:

- (1) You state that there is no safety concern related to skin irritation because the cells that make up the external layers of the nail are inert.
- (2) You argue that FDA's concern about using topical antifungal drug products labeled for prevention of jock itch indefinitely in the groin (54 FR 51136 at 51145-51146) does not apply to products labeled for the prevention of nail fungal infection.

FDA denies your petition because you have not provided adequate evidence to support the effectiveness of 1% tolnaftate in preventing nail fungal infections. Although you cite the tentative final monograph (TFM) for topical antifungal drug products (54 FR 51136) to support your request, we expressed safety and effectiveness concerns related to a nail fungal infection claim in the TFM and other *Federal Register* notices. In the Advance Notice of Proposed Rulemaking (ANPR) for topical antifungal drug products, the Advisory Review Panel on OTC Antimicrobial II Drug Products (the Panel) recommended excluding fungal infections of the scalp and nails in its discussion of ringworm (47 FR 12480 at 12487):

Fungal infections of the scalp and nails tend to be chronic. They respond poorly to topical therapy, partly because of the thickness of the nails and the depth of the hair roots. Both sites of infection provide inaccessible locations for fungi, thus drastically decreasing the penetration of topical antifungals. For this reason, OTC topical antifungals must be labeled that they are not effective for the treatment of ringworm of the scalp or nails.

Thus, the Panel recommended that all topical antifungal drug products labeled for the treatment of athlete's foot, jock itch, and ringworm include the following statement on their label: "This product is not effective on the scalp or nails" (47 FR 12480 at 12512). In the TFM, FDA agreed with the Panel and proposed requiring the statement recommended by the Panel (54 FR 51136 at 51155). FDA published a final rule on September 2, 1993, stating that use of OTC topical antifungal drug products on the nails or scalp is nonmonograph and placing this claim or directions for use as non-monograph in § 310.545(a)(22) (58 FR 46744). FDA's conclusion was reiterated in another final rule published on September 23, 1993, in which FDA stated that there is insufficient evidence to support the use of topical antifungal drug products for the treatment of nail or scalp fungal infection (58 FR 49890 at 49895). Because you did not submit any effectiveness data, we have no basis to recognize prevention of nail fungal infection as a GRASE indication for 1% tolnaftate.

For the foregoing reasons, FDA denies your petition. If you have any questions regarding this matter, please refer to the docket and comment numbers shown at the beginning of this letter and submit all inquiries in triplicate to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Maryland 20852.

Sincerely yours,



John M. Taylor, III  
Associate Commissioner  
for Regulatory Affairs