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Re: Docket 1978N-0065: Skin Bleaching Drug Products for OTC Human Use

To Whom It May Concern:

As a Professor and Chair of Dermatology at the Wake Forest University School of Medicine, I have substantial experience regarding hydroquinone and related products, including both over-the-counter and prescription products. I have personally seen multiple cases of exogenous ochronosis in my career related to use of these agents.

I strongly agree with FDA's decision to prohibit the OTC marketing of hydroquinone-containing skin-bleaching products, and I strongly believe that hydroquinone-containing drug products should not be able to enter the market unless and until they are approved by the FDA pursuant to a new drug application. The public and prescribing both community deserve appropriate safety and toxicity data to help make more informed decisions.

Based upon the current state of the science, the safest course is for each skin-bleaching product to be subject to product-specific safety and efficacy studies in order to ensure that patients obtain effective and safe therapies. I am aware that one hydroquinone-containing prescription drug products, Tri-Luma, has been FDA-approved and I am therefore comfortable prescribing it to my patients. Indeed, my University restricts my use of drugs to those approved by the FDA. Without such drug approval, I am required to submit a protocol to our Institutional Review Board for them to weigh the risks and benefits of unapproved therapies. FDA approval is highly important for we practitioners. I am also aware and was a primary investigator in the development of another product, Solag , which contains a hydroquinone-like drug, Mequinol, which has also been extensively studied and approved.

I am very concerned, however, that there may be a fundamental flaw in FDA's regulatory approach. FDA has indicated that it will require current OTC hydroquinone products to obtain NDA approval for prescription use in order to remain on the market. In practice, however, FDA has been exceedingly lax in enforcing NDA requirements against hydroquinone-containing prescription drugs. FDA has not enforced against these products, even though they contain ingredient combinations never reviewed by the FDA for safety and efficacy. I am deeply troubled by the fact that many dermatologic patients are currently being treated by prescription drugs that have never been evaluated by the FDA, let alone deemed safe and effective. This is particularly a problem because many physicians are simply unaware that these prescription drugs are

78N-0065

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Wake Forest University Health Sciences

unapproved - and they are operating under the assumption that safety and efficacy has been proven when this is not the case.

More importantly, I am troubled by the potential safety concerns that may emerge for my patients due to the unfettered expansion of product claims. The underlying premise of FDA regulation is that the risks of all drug products must be compared to product benefits. The benefit side of the equation is based upon product claims. To the extent, however, that FDA is currently permitting prescription hydroquinone drug products to be marketed in the absence of FDA approval, and such products are permitted to expand efficacy claims in labeling and advertising, serious problems emerge. Specifically, without FDA to compare the product risks against the claimed benefits of these products, these unapproved products may in fact pose unacceptable risks to your patients. This is simply an unacceptable regulatory outcome if the FDA's goal is to ensure that dermatologic drugs are safe and effective for patients.

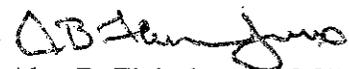
Unless FDA immediately enforces against unapproved prescription drugs containing hydroquinone, you are concerned that FDA's regulatory approach may have the exact opposite approach than the agency is envisioning. At present, under the OTC drug review, hydroquinone-containing OTC drugs are subject to claim limitations in order to be marketed in accordance with the OTC Drug Review. However, in the absence of FDA enforcement against unapproved hydroquinone-containing prescription drugs, there are no claim prohibitions. In other words, unless FDA enforces the NDA requirement, the ultimate result of this regulation may be the proliferation of unapproved claims for hydroquinone products that far exceed the claims currently made pursuant to the OTC drug review. This cannot be the result FDA intends to achieve.

In addition, in the absence of FDA enforcement against current unapproved hydroquinone-containing prescription drugs, the companies marketing OTC hydroquinone drugs will (perhaps correctly) assume that FDA will not enforce the NDA requirement - and these companies may therefore ignore the FDA approval process. This, again, cannot be the result FDA intends to achieve.

For all of the above reasons, it is imperative that FDA immediately enforce the NDA requirement for prescription drugs containing hydroquinone. Failure to enforce against these products will in essence expand the unfettered and unregulated use of product claims - with a potentially significant impact on patient safety.

I thank you for your consideration.

Sincerely



Alan B. Fleischer, Jr., M.D.  
Professor of Dermatology