CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-586

OFFICE DIRECTOR MEMO

NDA 21-586

Office Director Memo: Mark J Goldberger MD MPH

Product: DuraPrep Surgical Solution (Iodophor –0.7% available iodine) and Isopropyl Alcohol (74% w/v)

Indication: Patient Pre-Operative Skin Preparation

The results of the clinical studies and related investigations have been thoroughly discussed in reviews by Dr. Mulinde and Dr. Coderre and then summarized in a Division Director Memo by Dr. Soreth. that also provided the regulatory history of this product. For the patient preoperative skin preparation indication in the Tentative Final Monograph for Health Care Antiseptic Drug Products that include povidine iodine as a Category I active ingredient, a mean 2 log decrease in bacterial counts on the abdominal wall at 10 minutes is required. For the groin site a mean three log decrease in bacterial counts at the groin site at ten minutes is required. Also required is that bacterial counts at six hours remain below baseline counts. Because this product does not contain povidine iodine but a different iodophore it is not a monograph product and the sponsor was advised in 1994 that an NDA would be required.. The sponsor had submitted a citizen's petition requesting that they be treated as a monograph product. This has not been acted upon to date.

If one were to utilize the monograph standards it is clear that in two clinical trials the product met the required two log decrease in bacterial counts on the skin of the abdomen and that it did not show the required three log decrease in the groin. In one of the two trials the response at the groin site was only slightly below three logs (2.95). If this were the only criterion for an approval decision then recommending approval would be difficult. Consideration of the entire situation leads to a different conclusion.

From an efficacy perspective this product was compared in the above clinical trials to Hibiclens a chlorhexidine based product that is FDA approved for this indication and in wide usage. In the four possible comparisons vs Hibiclens at the ten minute time point this product was numerically better in all four and statistically significantly better in one of the two comparisons involving the groin. In addition the applicant performed two bacterial challenge studies to assess the contribution of the iodine component to the DuraPrep solution. These studies both showed a notable (statistically significant) increase in activity for the combination. Particularly striking was the dramatic increase in activity against Staphylococcus aureus an important cause of serious wound and post-operative infections.

In a June 2003 teleconference with the firm in which representatives of DAIDP and OTC participated the sponsor was told that they would not need to perform an additional clinical trial. They were told that the data from their two clinical trials if confirmed would be sufficient for approval. The status of this product as a new drug was confirmed at this meeting. Although a strict application of the standards in the TFM would likely have led to a different conclusion regarding the need for an additional trial this was not the advice the company was given.

This product is currently marketed without benefit of monograph or NDA. This will not change regardless of the approval decision.

Given the above my opinion is as follows:

The available data support the activity of this product for pre-operative skin preparation. The advice given in June 2003 is I believe consistent with the statutory standard requiring substantial evidence of safety and efficacy for the approval of a new drug. In any case no new scientific information has come forth to justify a change in that advice and therefore I cannot see the basis for modifying it.

This product is currently being marketed. As a matter of policy I believe it appropriate to have such a product marketed whenever possible under an NDA to facilitate such issues as potential CMC, and labeling changes and related issues. Leaving it in its current state of limbo seems in no one's interest.

I recognize the concerns about the precedent this might establish for similar products under a monograph. I believe that is not a major concern for this product as it is an NDA not a monograph product, is accompanied by additional scientific studies beyond the required two clinical trials and is accompanied by substantial post-marketing experience.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Edward Cox
8/26/04 01:07:56 PM
MEDICAL OFFICER

for Mark J. Goldberger, MD MPH