

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*  
**NDA 19-422 / S-032**

**CLINICAL CONSULTATIVE REVIEW(S)**

Addendum to Clinical Consultative Review of Efficacy Supplement

NDA 19-422/S-032

Date of Submission: July 15, 2002

Date Assigned to Reviewer: September 10, 2002

Date of Review Initiation: September 12, 2002

Drug: Exidine (chlorhexidine gluconate 2%) solution) Antiseptic

Applicant: Xttrium Laboratories  
Chicago, IL 60609

Reason for Addendum: The applicant has asked for a waiver of the requirement for pediatric studies for this product.

Background: This supplement was originally submitted on January 10, 2002 and was reviewed in a Clinical Review dated August 5, 2002. Under the requirements of the Pediatric Rule, the sponsor is required to either submit pediatric studies concerning the indication addressed in the efficacy supplement, or submit a request for a waiver of such studies. The attached Pediatric Page provides an evaluation of the need for pediatric studies to support this supplement.

\_\_\_\_\_  
David C. Bostwick

\_\_\_\_\_  
Jean Mulinde, MD

HFD-520/Bostwick  
HFD-520/DivDir/Soreth  
HFD-520/TL/Mulinde  
HFD-960/Crescenzie

**PEDIATRIC PAGE**

NDA No. 19-422 Supplement Type: SE-2 Supplement Number : 032

Stamp Date: January 10, 2002 Action Date:

HFD 520 Trade and generic names/dosage form: Exidine (chlorhexidine gluconate  
2% solution) Antiseptic

Applicant: Xttrium Laboratories Chicago, IL 60609 Therapeutic Class: 3C

Indication (s) previously approved: Surgical hand scrub; healthcare personnel handwash;  
patient preoperative skin preparation/skin wound and general skin cleansing.

Number of Indications for this application: 1

Indication #1: Surgical hand scrubbing

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No:

**Section A: Fully Waived Studies**

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Often

Note: This supplement does not concern the other approved indications for the drug.

This page was completed by David Bostwick, HFD-520.

Clinical Consultative Review of Efficacy Supplement  
NDA 19-422/S-032

Date of Consult Request: None

Date HFD-520 Received: Not known; originally sent to HFD-520 chemist (Dr. Shetty) on March 4, 2002.

Date Assigned to Reviewer: June 1, 2002

Date of Submission: January 10, 2002

Date CDER Received: February 25, 2002

Date of Review Initiation: August 5, 2002

Drug: Exidine (chlorhexidine gluconate 2% solution) Antiseptic

Applicant: Xttrium Laboratories, Inc.  
Chicago, Illinois 60609

Indications: Surgical hand scrub; healthcare personnel handwash; patient preoperative skin preparation/skin wound and general skin cleansing.

Reasons for supplement: Revisions in the directions for use for the product as a surgical hand scrub, providing for two 1.5 minute scrubs rather than the presently approved two 3 minute scrubs. In addition, the revised directions recommend use of 8 mL of the product per scrub, rather than 5 mL, and permit scrubbing without use of a scrub brush.

The labeling has also been generally updated to meet current standards for OTC chlorhexidine gluconate products.

Background: The clinical simulation study submitted in support of this supplement (\_\_\_\_\_ Study No. 010206-102) is the same study that was submitted in support of \_\_\_\_\_. That supplement was reviewed by Mr. Bostwick and Dr. Makhene in a review dated September 13, 2001. A copy of that document is attached. \_\_\_\_\_ was withdrawn by the sponsor on January 23, 2002 for unspecified reasons. Similar material, including the identical clinical simulation study report, was submitted on January 10, 2002 (but not received by CDER until February 25, 2002) and was designated as supplement no. 032. Therefore, reference is made to the attached review of \_\_\_\_\_ for review of the efficacy study. The labeling which is submitted with S-032 is slightly revised from that submitted with \_\_\_\_\_. Please see the following Review of Labeling and Conclusions and Recommendations.

### 1. Review of Labeling

The following revisions are necessary for the labeling submitted January 10, 2002 with S-032:

- a. The front panel of the labeling (identified by the sponsor as "Principle (sic) Display Panel") is not satisfactory in that it is general in presentation. That is, rather than giving the name of the product as Exidine, the label states "\_\_\_\_\_". Similarly, rather than giving the manufacturer's name as Xttrium, the label states "\_\_\_\_\_". It is the understanding of the reviewers that the Division of OTC Drug Products, which is also reviewing the labeling, has already contacted the sponsor concerning this deficiency.
- b. The "Uses" subsection of the labeling should be revised as follows:
  - i. The "patient preoperative skin preparation" and "skin wound and general skin cleansing" statement should be separated.
  - ii. The patient preoperative skin preparation statement should be followed by "for the preparation of the patient's skin prior to surgery."
  - iii. The skin wound and general skin cleansing statement should not have any explanatory material following it. This indication is no longer granted for products of this type, and the benefits of this use are not clear.
- c. In the "Stop use and ask doctor" subsection, the phrase "\_\_\_\_\_" should be deleted.
- d. In the "Directions" for use as a surgical hand scrub, the following revisions should be made:
  - i. The first bullet should read, "Wet hands and forearms under running water for 30 seconds. Clean fingernails using a nailstick or similar cleaner."
  - ii. The fourth bullet should read, "Rinse thoroughly under running water for 30 seconds."
  - iii. The fifth bullet should read, "Wash for an additional 1.5 minutes with 8 mL of product and rinse under running water for 30 seconds."

### 2. Conclusions and Recommendations

This supplemental application maybe approved from a clinical standpoint. However, before action is taken, the following items are necessary:

- a. A favorable review from HFD-520 microbiology personnel.
- b. Revised labeling as specified above.

David C. Bostwick

Jean Mulinde, MD

ATTACHMENT

HFD-520/TL/Mulinde  
HFD- 520/Div Dir/Soreth  
HFD-520/Micro/Sheldon  
HFD-520/Frazier  
HFD-520/Ganley

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CLINICAL CONSULTATIVE REVIEW (ATTACHMENT)

2. Revised labeling as specified above.

\_\_\_\_\_  
David C. Bostwick

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Mamodikoe Makhene, M.D.

HFD-520  
HFD-520/Bostwick  
HFD-520/Makhene  
HFD-560/Katz  
HFD-560/Jackson  
Orig NDA

Concurrence only:  
HFD-520/Acting DivDir/Soreth

**APPEARS THIS WAY  
ON ORIGINAL**