



NDA 18-634/S-007

Alcon Universal, Ltd.
c/o Alcon Research, Ltd.
Attn: Norma J. Schafer
Regulatory Affairs Analyst
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Ms. Schafer:

Please refer to your supplemental new drug application dated November 1, 2002, received November 4, 2002, submitted under of the Federal Food, Drug, and Cosmetic Act for Betadine (povidone-iodine ophthalmic solution) 5%.

This "Changes Being Effected" supplemental new drug application provides for a Geriatric Use subsection under the **PRECAUTIONS** section and other changes to the product package insert.

We completed our review of this supplemental new drug application. It is are approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on November 1, 2002.

If a future supplement is submitted, the following revisions should be made:

The pH and osmolality should be added to the **DESCRIPTION** section of the package insert.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Lori M. Gorski, Regulatory Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

Betadine® 5%

Sterile Ophthalmic

Prep Solution

(povidone-iodine ophthalmic solution)

(0.5% available iodine)

DESCRIPTION: Povidone-Iodine is a broad-spectrum microbicide with the chemical formulas: 2-pyrrolidinone, 1-ethenyl-, homopolymer, compound with iodine; 1-vinyl-2-pyrrolidinone polymer, compound with iodine. The structural formula is as follows:

[structure]

BETADINE® 5% Sterile Ophthalmic Prep Solution contains 5% povidone-iodine (0.5% available iodine) as a sterile dark brown solution stabilized by glycerin. Inactive Ingredients: citric acid, glycerin, nonoxynol-9, sodium chloride, sodium hydroxide, and dibasic sodium phosphate.

CLINICAL PHARMACOLOGY: A placebo-controlled study in 38 normal volunteers yielded data for 36 subjects who showed a mean \log_{10} reduction of 3.05 \log_{10} units in total aerobes at 10 minutes following prepping the skin with BETADINE 5% Sterile Ophthalmic Prep Solution compared with reduction of 1.58 \log_{10} units after prepping with vehicle free of the iodine complex. This placebo-controlled study indicates a mean \log_{10} reduction by the iodine complex compared with the control solution of 1.47 \log_{10} units at 10 minutes and 1.79 \log_{10} units at 45 minutes. The base-line mean aerobic bacterial count was 7,586 organisms per square cm.

INDICATIONS AND USAGE: BETADINE 5% Sterile Ophthalmic Prep Solution for the eye is indicated for prepping of the periocular region (lids, brow, and cheek) and irrigation of the ocular surface (cornea, conjunctiva, and palpebral fornices).

CONTRAINDICATIONS: Do not use on individuals known to be sensitive to iodine, or other components of this product.

WARNINGS: FOR EXTERNAL USE ONLY. NOT FOR INTRAOCULAR INJECTION OR IRRIGATION.

PRECAUTIONS:

General: No studies are available in patients with thyroid disorders; therefore, caution is advised in using BETADINE 5% Sterile Ophthalmic Prep Solution in these patients due to the possibility of iodine absorption.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No long term studies in animals have been performed to evaluate the carcinogenic or mutagenic potential of povidone-iodine. One report of the mutagenic potential of povidone-iodine indicated that it was positive in a modification of the Ames S. typhimurium model, but these results could not be reproduced by another researcher. Another test using mouse lymphoma and Balb/3T3 cells showed that povidone-iodine has no significant mutagenic or transformation capabilities. Other data indicated that it does not produce mutagenic effects in mice or hamsters according to the dominant lethal test, micronucleus test, and chromosome analysis.

Pregnancy Category C: Animal reproduction studies have not been conducted with BETADINE® 5% Sterile Ophthalmic Prep Solution. It is also not known whether BETADINE 5% Sterile Ophthalmic Prep Solution can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. BETADINE 5% Sterile Ophthalmic Prep Solution should only be used on a pregnant woman if clearly needed.

Nursing Mothers: Because of the potential for serious adverse reactions in nursing infants from BETADINE 5% Sterile Ophthalmic Prep Solution, a decision should be made to discontinue nursing or discontinue the drug taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use: No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS: Local sensitivity has been exhibited by some individuals to povidone-iodine ophthalmic solution.

DOSAGE AND ADMINISTRATION: While the inner surface and contents of the immediate container (i.e. bottle) are sterile, the outer surface of the bottle is not sterile. The use of the bottle in a sterile field should be avoided.

BETADINE 5% Sterile Ophthalmic Prep Solution is used as follows:

1. Make sure container is intact before use. To open, COMPLETELY TWIST OFF TAB, do not pull off. Gently squeeze entire contents of bottle into a sterile prep cup.
2. Saturate sterile cotton-tipped applicator to prep lashes and lid margins using one or more applicators per lid; repeat once.
3. Saturate sterile prep sponge or other suitable material to prep lids, brow and cheek in a circular ever-expanding fashion until the entire field is covered; repeat prep three (3) times.
4. While separating the lids, irrigate the cornea, conjunctiva and palpebral fornices with BETADINE 5% Sterile Ophthalmic Prep Solution using a sterile bulb syringe.
5. After the BETADINE 5% Sterile Ophthalmic Prep Solution has been left in contact for two minutes, sterile saline solution in a bulb syringe should be used to flush the residual prep solution from the cornea, conjunctiva, and the palpebral fornices.

HOW SUPPLIED: BETADINE 5% Sterile Ophthalmic Prep Solution is packaged under sterile conditions and supplied in 1 fl.oz. (30 mL) form sealed blue HDPE bottles (NDC #0065 0411 30). Twenty-four (24) bottles are packed in each shipper.

Store at 15-25° C (59-77° F).

Rx Only

Single use only

Alcon®

Manufactured for:
Alcon Laboratories, Inc.
Fort Worth, TX 76134

Manufactured by:
Automatic Liquid Packaging, Inc.
Woodstock, IL 60098
BETADINE® is a registered trademark of
The Purdue Frederick Company.

BETAGER-0802

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/s/

Wiley Chambers
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