CYSTARAN™ (CYSTEAMINE OPHTHALMIC SOLUTION) 0.44% STERILE

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use CYSTARAN™ safely and effectively. See full prescribing information for CYSTARAN.

1 INDICATIONS AND USAGE

CYSTARAN is a cystine-depleting agent indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis. (1)

2 DOSAGE AND ADMINISTRATION

Instill one drop of CYSTARAN in each eye, every waking hour. (2)

3 DOSAGE FORMS AND STRENGTHS

STERILE ophthalmic solution containing 6.5 mg/mL of cysteamine hydrochloride equivalent to 4.4 mg/mL of cysteamine (0.44%). (3)

4 CONTRAINDICATIONS

None. (4)

5 WARNINGS AND PRECAUTIONS

To avoid contamination, do not touch dropper tip to any surface. Keep bottle tightly closed when not in use. (5.1)

6 ADVERSE REACTIONS

Variations in adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety data described below reflect exposure in controlled clinical trials of six months to 19 years compared to rates in the clinical trials of another drug. The most frequently reported ocular adverse reactions occurring in >10% of patients were sensitivity to light, redness, eye pain/irritation, headache and visual field defects. (6)

7 USE IN SPECIFIC POPULATIONS

Clinical Studies Experience

There are no adequate and well-controlled studies of CYSTARAN in pregnant women. CYSTARAN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. (8.1)

Teratogenic Effects: Pregnancy Category C.

Teratology studies have been performed in rats at oral doses in a range of 37.5 mg/kg/day to 150 mg/kg/day (about 0.2 to 0.7 times the recommended human maintenance dose on a body surface basis) and have revealed cysteamine bitartrate to be teratogenic. Observed teratogenic findings were cleft palate, kyphosis, heart ventricular septal defects, microphthalmia, and exencephaly. (8.1)

Nonteratogenic Effects: Cysteamine was fetotoxic, resulting in intrauterine death and growth retardation in rats at oral doses of 0.2 to 0.7 times the recommended human maintenance dose on a body surface basis. (8.3)

ADVERSE REACTIONS

The most common adverse reactions (incidence approximately 10% or greater) are sensitivity to light, redness, eye pain/irritation, headache and visual field defects. (6)

13 NONCLINICAL TOXICOLOGY

Recombinant Human Cysteamine bitartrate has been shown to be nonteratogenic and nonmutagenic in animal studies. (13.1)

17 PATIENT COUNSELING INFORMATION

See 17 for PATIENT COUNSELING INFORMATION Revised: [10/2012]

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*Sections or subsections omitted from the full prescribing information are not listed.
Cysteamine acts as a cystine-depleting agent by converting cystine to cysteine and cysteine-mixed disulfides and reduces corneal cystine crystal accumulation.

12.3 Pharmacokinetics

The peak plasma concentration of cysteamine following topical administration of cysteamine ophthalmic solution in humans is unknown, but it is expected to be substantially less than the peak plasma concentration following oral administration of cysteamine bitartrate.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Cysteamine has not been tested for its carcinogenic potential in long-term animal studies. Cysteamine was not mutagenic in the Ames test. It produced a negative response in an in vitro sister chromatid exchange assay in human lymphocytes but a positive response in a similar assay in hamster ovarian cells.

Repeat breeding reproduction studies were conducted in male and female rats. Cysteamine was found to have no effect on fertility and reproductive performance at an oral dose of 75 mg/kg/day (430 mg/kg/day, 0.4 times the recommended human dose based on body surface area). At an oral dose of 375 mg/kg/day (2,250 mg/kg/day, 1.7 times the recommended human dose based on body surface area), it reduced the fertility of the adult rats and the survival of their offspring.

14 CLINICAL STUDIES

Clinical efficacy was evaluated in controlled clinical trials in approximately 300 patients. The primary endpoint of the study was the response rate of eyes that had a reduction of at least 1 unit in the photo-rated Corneal Cystine Crystal Score (CCCS) at some time period during the study when baseline CCCS > 1, or a lack of an increase of more than 1 unit in CCCS throughout the study when baseline CCCS < 1.

Study 1 evaluated ocular cystinosis patients who had a baseline of CCCS > 1. The response rate was 32% (94/291) [95% CI: (27, 38)].

Study 2 also evaluated ocular cystinosis patients; for eyes with a baseline of CCCS ≤ 1, the response rate was 33% (3/9) [95% CI: (8, 70)].

Corneal crystals accumulate if CYSTARAN is discontinued.

16 HOW SUPPLIED/STORAGE AND HANDLING

Cysteamine ophthalmic solution (0.44%) is supplied in a 15 mL, opaque, white, low-density polyethylene (LDPE) bottle with a 15 mm white, LDPE controlled dropper tip and closed with a white, polystyrene screw cap.

Storage: Store in freezer at -25°C to -15°C (-13°F to 5°F). Thaw for approximately 24 hours before use. Store thawed bottle at 2°C to 25°C (36°F to 77°F) for up to 1 week. Do not refreeze. Discard after 1 week of use.

17 PATIENT COUNSELING INFORMATION

17.1 Storage of Bottles

1. Patients should be advised to store bottles in the freezer in the original carton.

2. Each week, one new bottle should be removed from the freezer.

3. Patients should be advised to allow the bottle to thaw completely (approximately 24 hours) prior to use.

4. After the bottle is completely thawed, the patient should record the discard date on the bottle label. The discard date is seven (7) days from the day the bottle is thawed.

5. Patients should be advised to store thawed bottle at 2°C to 25°C (36°F to 77°F) for up to 1 week. The thawed bottles should not be refrozen.

6. At the end of 1 week (7 days), patients should discard the bottle. There may be medication left in the container. The bottle must be discarded by the patient because the medication is only stable for 1 week after thawing.

17.2 Risk of Contamination

Patients should be advised not to touch the eyelid or surrounding areas after touching the dropper tip of the bottle. The cap should remain on the bottle when not in use.

17.3 Use with Contact Lenses

Patients should be advised that contact lenses should be removed prior to application of CYSTARAN. Contact lenses may be inserted 15 minutes following CYSTARAN administration.

17.4 Topical Ophthalmic Use Only

Patients should be advised that CYSTARAN is for topical ophthalmic use only.