PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrCYSKLAR™

Cysteamine Ophthalmic Solution

For ophthalmic use

0.44% w/v cysteamine (as cysteamine hydrochloride)

Cystine-Depleting Agent

Leadiant Biosciences, Inc.

16-2000 Ellesmere Road

Scarborough, ON M1H 2W4

Date of Authorization:
2026-03-06

Submission Control Number: 285212

RECENT MAJOR LABEL CHANGES

None at time of authorization.

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Sections or subsections that are not applicable at the time of the most recent authorized product monograph are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

CYSKLAR™ (*cysteamine ophthalmic solution*) is indicated for:

- the treatment of corneal cystine crystal accumulation in patients with cystinosis.

1.1 Pediatrics

Pediatrics (< 18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of CYSKLAR in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use. (see 14 CLINICAL TRIALS)

1.2 Geriatrics

Geriatrics (> 65 years of age): No data are available to Health Canada; therefore, the safety and efficacy are not established for geriatric use.

2 CONTRAINDICATIONS

CYSKLAR is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Treatment with CYSKLAR should be initiated under the supervision of a physician experienced in the management of cystinosis.

4.2 Recommended Dose and Dosage Adjustment

- The recommended dose is one drop of CYSKLAR in each eye, every waking hour.
- CYSKLAR may be used in pediatric (< 18 years of age) patients at the same dose as in adults (see 14 CLINICAL TRIALS).

4.4 Administration

- For ophthalmic use.
- Before opening, the patient should be advised to store CYSKLAR in the refrigerator in the original carton and unopened foil.
- The patient should be advised to open the carton and foil only when starting a new bottle. After opening, store bottle at room temperature. The bottle does not require refrigeration between use (see 11 STORAGE, STABILITY, AND DISPOSAL).
- The patient should be advised not to touch the eyelid or surrounding areas with the dropper tip of the bottle, as this may contaminate the solution. The cap should remain on the bottle when not in use.
- Patients should be advised that contact lenses should be removed prior to application of CYSKLAR. Contact lenses may be inserted 15 minutes following administration.

- The patient should be advised to discard the bottle after 1 week of use.

4.5 Missed Dose

If a dose is missed, the patient should be advised to continue the treatment with the next instillation.

5 OVERDOSE

If the patient administers too much CYSKLAR, allow a few minutes for blinking of the eyes. If irritation or pain persists, instruct patient to rinse out the eye(s) with an ophthalmic saline or buffered solution. No further drops should be administered until it is time for the next regular dose.

Systemic overdose is unlikely to occur with ocular administration.

In case of accidental ingestion, patient should contact their physician. Monitoring and symptomatic management of the patient should be implemented.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths and Composition

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Ophthalmic	Solution containing 6.5 mg/mL cysteamine hydrochloride equivalent to 4.4 mg/mL of cysteamine (0.44% w/v)	benzalkonium chloride hydrochloric acid sodium chloride sodium hydroxide water for injection

Fifteen (15) mL of CYSKLAR is supplied as a sterile, clear, colorless solution in a 23.24 mL, opaque, white, low-density polyethylene (LDPE) 88.2 mm tall, multi-use bottle, with a 1.6 mm blue, silicone rubber flow-controlled dropper tip and closed with a white, high-density polyethylene (HDPE) screw cap. The bottle is foil-wrapped and stored in a carton.

7 WARNINGS AND PRECAUTIONS

General

For ophthalmic use only.

To minimize contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

Driving and Operating Machinery

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines.

If blurred vision occurs after administration, the patient must wait until their vision clears before driving or using dangerous machinery.

Neurologic

Benign Intracranial Hypertension

There have been reports of benign intracranial hypertension (or pseudotumor cerebri) associated with oral cysteamine treatment that has resolved with the addition of diuretic therapy.

There have also been reports associated with ophthalmic use of cysteamine; however, all of these patients were on concurrent oral cysteamine.

Ophthalmologic

CYSKLAR contains benzalkonium chloride which may cause eye irritation.

Benzalkonium chloride, which is commonly used as a preservative in ophthalmic products has also been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Monitoring is required.

Contact Lens Use

CYSKLAR contains benzalkonium chloride, which may be absorbed by soft contact lenses. Benzalkonium chloride is known to discolour soft contact lenses. Contact with soft contact lenses should be avoided. Contact lenses should be removed prior to application of solution and may be reinserted 15 minutes following its administration.

Reproductive Health

Fertility

No data on the effect of cysteamine on human fertility are available. Studies in animals with cysteamine administered orally have shown a reduction of fertility (see 16 NON-CLINICAL TOXICOLOGY).

7.1 Special Populations

7.1.1 Pregnant Women

There are no adequate and well controlled studies of ophthalmic cysteamine in pregnant women to inform any drug associated risks. CYSKLAR should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus and should be discussed with the primary provider.

The recommended total daily ophthalmic dose of CYSKLAR is less than 2% of the recommended oral daily dose of cysteamine. Systemic exposure of cysteamine following ophthalmic administration is expected to be very low.

Studies in animals with oral cysteamine have shown reproductive toxicity, including teratogenesis. The potential risk in humans is unknown (see 16 NON-CLINICAL TOXICOLOGY).

7.1.2 Breastfeeding

There is no information regarding the presence of cysteamine in human milk, the effects on the breastfed infants, or the effects on milk production.

Cysteamine administered orally is present in milk of lactating rats. It is not known whether measurable levels of cysteamine would be present in maternal milk following topical ocular administration of cysteamine ophthalmic solution. Oral administration of cysteamine to breast-feeding mother rats reduced growth and increased mortality rates among their neonates (see 16 NON-CLINICAL TOXICOLOGY).

It is unknown if CYSKLAR is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

7.1.3 Pediatrics

The safety and effectiveness of CYSKLAR have been established in pediatric patients (< 18 years of age) at the same dose as adults (see 14 CLINICAL TRIALS).

7.1.4 Geriatrics

Geriatrics (> 65 years of age): No data are available to Health Canada; therefore, the safety and efficacy are not established for geriatric use.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Safety data was collected from 3 controlled clinical studies in adult and pediatric patients. The mean study duration was approximately 6 years in Study 1. Study 2 and 3 had a duration of 1 year and 6 months, respectively.

The most frequently reported adverse reactions occurring in ≥10% of patients from clinical studies were sensitivity to light, eye redness, eye pain/irritation, instillation site redness/irritation/pain, headache and visual field defects.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

Study 1 is a combined analysis of three smaller controlled clinical studies which evaluated several formulations of ophthalmic cysteamine solution. Table 2 outlines the incidence of the most common (≥1%) adverse events in the safety population in Study 1. The safety population consisted of 247 patients (adult and pediatric patients ranged in age from <1 year to 49.6 years). The mean (±SD) treatment duration was 5.8 ± 5.5 years.

Table 2 Summary of the Incidence of the Most Common (≥1%) Adverse Events (AE) (n and %) for the Treatment Period – Safety Population (Study 1)

System Organ Class[a] Preferred Term[a]	**Total (N = 247)** **n (%)**
Number of Patients With at Least One AE	**169 (68.4)**
Eye Disorders	**166 (67.2)**
Photophobia	157 (63.6)
Conjunctival Hyperaemia	69 (27.9)
Eye Pain	48 (19.4)
Ocular Hyperaemia	43 (17.4)
Eye Irritation	42 (17.0)
Lacrimation Increased	21 (8.5)
Keratitis	19 (7.7)
Optic Disc Disorder	18 (7.3)
Vision Blurred	17 (6.9)
Dry Eye	13 (5.3)
Eyelid Oedema	12 (4.9)
Retinal Disorder	11 (4.5)
Conjunctivitis	10 (4.0)
Eye Pruritus	10 (4.0)
Blindness	7 (2.8)
Corneal Epithelium Disorder	6 (2.4)
Blepharitis	5 (2.0)
Erythema of Eyelid	5 (2.0)
Eye Swelling	3 (1.2)
Nervous System Disorders	**63 (25.5)**
Headache	34 (13.8)
Visual Field Defect	32 (13.0)
Benign Intracranial Hypertension	8 (3.2)
General Disorders and Administration Site Conditions	**45 (18.2)**
Instillation Site Irritation	30 (12.1)
Instillation Site Pain	17 (6.9)
Adverse Drug Reaction	7 (2.8)

Table 2 Summary of the Incidence of the Most Common (≥1%) Adverse Events (AE) (n and %) for the Treatment Period – Safety Population (Study 1)

System Organ Class[a] Preferred Term[a]	**Total (N = 247)** **n (%)**
Instillation Site Erythema	5 (2.0)
Infections and Infestations	**11 (4.5)**
Eye Infection	5 (2.0)
Conjunctivitis Infective	3 (1.2)
Hordeolum	3 (1.2)
Gastrointestinal Disorders	**8 (3.2)**
Vomiting	8 (3.2)

[a]All AE terms were coded using MedDRA Dictionary Version 9.0.
Note: A patient experiencing multiple occurrences of an AE is counted only once within each system organ class and within each preferred term.

Study 2 was a multicenter, randomized, double masked, comparative safety and efficacy trial comparing two formulations of the cysteamine ophthalmic solution over a 12-month treatment period. Safety population consisted of 16 pediatric patients.

Study 3 was a single center, randomized, double masked, comparative safety and efficacy trial comparing 2 formulations of the cysteamine ophthalmic solution over a 6-month treatment period. The safety population consisted of 20 adult and pediatric patients.

The safety profile of CYSKLAR in supportive Studies 2 and 3 is consistent with Study 1.

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

Pediatric patients are included in the clinical trials noted above. Table 3 outlines age distribution of pediatric patients in the clinical trials.

Table 3 Age Distribution of Pediatric Patients in the Clinical Trials

Study	Number of Pediatric Patients		
	Age 0 - <2 Years	Age 2 - <12 Years	12 - <18 Years
Study 1	23	93	60
Study 2	0	15	1
Study 3	0	9	9

8.3 Less Common Clinical Trial Adverse Reactions

The list includes less common clinical trial adverse reactions reported for adult and pediatric patients:

Eye Disorders: Conjunctival oedema, eye oedema, eyelid cyst, eyelid irritation, ulcerative keratitis
General Disorders and Administration Site Conditions: Drug ineffective, instillation site lacrimation, instillation site reaction
Immune System Disorders: Drug hypersensitivity
Investigations: Visual evoked potentials abnormal

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

No clinically relevant changes in laboratory findings were observed.

Post-Market Findings
No clinically relevant changes in laboratory findings were observed.

8.5 Post-Market Adverse Reactions

In the post-market setting CYSKLAR demonstrates an adverse event profile consistent with what was reported in the clinical trials.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No clinical drug interaction studies with CYSKLAR have been performed.

9.3 Drug-behaviour interactions

The interaction of CYSKLAR with individual behavioural risks (e.g. cigarette smoking, cannabis use, and/or alcohol consumption) has not been studied.

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Cysteamine acts as a cystine-depleting agent by converting cystine to cysteine and cysteine-cysteamine mixed disulfides and thereby reducing corneal cystine crystal accumulation.

10.2 Pharmacodynamics

Conventional pharmacodynamic studies using topically administered cysteamine have not been conducted.

10.3 Pharmacokinetics

Human pharmacokinetic studies were not conducted with cysteamine ophthalmic solution 0.44%.

The peak plasma concentration of cysteamine following ocular 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.

Cysteamine distribution, metabolism and excretion data were based on mode of administration that were not ophthalmic. Cysteamine that reach the systemic circulation upon ophthalmic administration is expected to be rapidly absorbed, distributed, metabolised and excreted in a similar manner, but tissue concentrations is expected to be low based on the low dose administered.

Special Populations and Conditions

Renal impairment: The effect of renal impairment on the pharmacokinetics of cysteamine following ophthalmic administration of cysteamine ophthalmic solution has not been evaluated in a dedicated renal impairment study.

The majority of the patients in the ophthalmic clinical studies are assumed to have had some degree of renal impairment due to their underlying systemic disease.

The total daily ophthalmic dose is less than 2% of the recommended oral daily dose of cysteamine; thus, the systemic exposure following ophthalmic administration is expected to be negligible compared to oral administration.

11 STORAGE, STABILITY AND DISPOSAL

Before Opening: Store unopened bottle in a refrigerator (2°C to 8°C) in the original packaging including unopened foil.

Open the carton and the foil only when starting a new bottle.

After Opening: Record opening date on the bottle. During the week of use, store bottle at room temperature, 20°C to 25°C. Discard 1 week after the foil and bottle were opened even if there is medication left in the bottle.

12 SPECIAL HANDLING INSTRUCTIONS

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

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

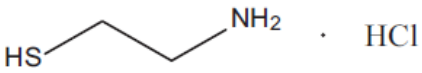
Drug Substance

Non-proprietary name of the drug substance: Cysteamine Hydrochloride

Chemical name: 2-Amino-ethanethiol hydrochloride/2-Mercaptoethylamine hydrochloride

Molecular formula and molecular mass: C_2H_7NS, HCl; 113.61

Structural formula:



Physicochemical properties:

Appearance: White to off-white solid.

Solubility: Freely soluble in water and soluble in 2-propanol at 20 °C.

pH: The pH of a 1% solution of Cysteamine HCl in water is 4.2 - 4.7.

Melting Point: 71.8°C.

Hygroscopicity: Cysteamine HCl will deliquesce at standard temperature and humidity conditions.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Table 4 - Summary of patient demographics for clinical trials in the treatment of corneal cystine crystal accumulation in patients with cystinosis

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Average age (Range)	Sex
Study 1	Randomized, Double-Masked	Placebo (saline) Formulation 1[a] Formulation 2[b] Formulation 3[c] (CYSKLAR) Formulation 4[d] One drop of cysteamine was administered to one eye and one drop placebo administered to companion eye, every waking hour; the administration was later amended to apply active treatment to both eyes. Duration of treatment: up to 19 years.	247 patients	13.8 years (< 1 to 49.6 years)	130 (52.6%) patients were male
Study 2	A Multicenter, Randomized, Double-Masked, Comparative Efficacy Trial	Formulation 3[c] (CYSKLAR) Formulation 5[e] One drop of Formulation 3 was administered to one eye and one drop of Formulation 5 was administered to the companion eye, every waking hour. Duration of treatment: up to 1 year.	16 patients	6.5 years (2.7-12.0 years)[f]	8 (50%) patients were male
Study 3	A Single-Center, Randomized, Double-Masked, Comparative Safety and Efficacy Trial	Formulation 3[c] (CYSKLAR) Formulation 5[e] One drop of Formulation 3 was administered to one eye and one drop of Formulation 5 was administered to the companion eye, every waking hour for 6 months	20 patients	13.4 years (5.9-27.8 years)[f]	13 (65.0%) patients were male

BAK = Benzalkonium chloride
[a]Formulation 1: 0.07% cysteamine (equivalent to 1.1 mg/mL cysteamine hydrochloride)
[b]Formulation 2: 0.44% cysteamine (equivalent to 6.5 mg/mL cysteamine hydrochloride)
[c]Formulation 3: 0.44% cysteamine (equivalent to 6.5 mg/mL cysteamine hydrochloride), 0.01% BAK
[d]Formulation 4: 0.55% cystamine , 0.01% BAK
[e]Formulation 5: 0.37% cysteamine (equivalent to 5.5 mg/mL cysteamine hydrochloride), BAK, monobasic sodium phosphate, EDTA
[f] All patients were of white, non-Hispanic origin

Study 1 combined data from three protocols and evaluated three (3) formulations of ophthalmic cysteamine solution (Formulations 1, 2 and 3) and one formulation of ophthalmic cystamine solution (Formulation 4). All patients who continued to participate in the study eventually switched to receiving Formulation 3 (CYSKLAR) in both eyes until the end of study. Of the 247 patients enrolled in the study, 161 (65.2%) were included in the efficacy analysis. Patients in the study ranged in age from < 1 year to 49 years with a mean (±SD) exposure to treatment of 5.8 ± 5.5 years. Mean (±SD) study duration for the analysis population was 8.5 ± 4.9 years. Patients were randomly assigned to treatment; all study participants and study staff were masked to the treatment administered. Patients received one drop of the assigned ophthalmic solution (Formulation 1, 2, 3, 4, or placebo) in the appropriate eye every waking hour. The primary endpoint was the reduction of corneal cystine crystal score (CCCS) in eyes with high CCCS (≥1) at baseline, and lack of increase in CCCS in eyes with low CCCS (<1) at baseline. A response was defined as a decrease from baseline of at least 1 unit in CCCS at any time on study when baseline CCCS was ≥1, or CCCS did not increase at least 1 unit at any time on study when baseline CCCS was <1.

For eyes with baseline CCCS ≥1, the response rate was 32% [95% CI: (27, 38)]. For eyes with baseline CCCS <1, the response rate was 13% [95% CI: (4, 31)]. For eyes with baseline CCCS ≥1, mean baseline CCCS score was 2.7 ± 0.5 (mean ± SD) with mean change of -0.2 ± 0.8 at Year 1. For eyes with baseline CCCS <1, mean baseline CCCS score was 0.3 ± 0.2 (mean ± SD) with mean change of 0.3 ± 0.5 at Year 1.

Study 2 was a multi-center, double masked, clinical trial. A total of 16 patients were randomized to receive one drop of Formulation 3 (CYSKLAR) in one eye and one drop of Formulation 5 (0.37% cysteamine, EDTA and BAK) in the companion eye every waking hour. Study investigators and all clinic staff were to be masked to treatment assignments. Patients enrolled were ranged from 2 to12 years of age (inclusive) who had never used cysteamine eye drops. The treatment duration was 1 year. All eyes evaluated in the study had CCCS baseline value ≥1.00. The primary efficacy end point was defined as the estimated proportion of eyes with a reduction of 1.00 unit or more in CCCS relative to at any time during the treatment period (up to Month 12) and at the specified time points of Months 3, 6, 9, and 12.

CYSKLAR response rate was 67% [95% CI: (38, 88)] at any time during the study. Mean baseline CCCS score for eyes receiving CYSKLAR was 2.7 ± 0.4 (mean ± SD) with mean change of -0.6 ± 0.7, -1.0 ± 0.9, -1.2 ± 1.0, and -0.9 ± 0.9 at Months 3, 6, 9, and 12, respectively.

Study 3 was a single-centre, double masked, randomized, comparative safety and efficacy study in, pediatric (≥ 1 year of age) and adult patients diagnosed with cystinosis. A total of 20 patients were randomized to receive one drop of Formulation 3 (CYSKLAR) in one eye and one drop of Formulation 5 in the companion eye every waking hour. Safety and efficacy assessments were done at baseline and at 6 months. The study duration was 6 months and the efficacy analysis was conducted at 6 months in the per protocol population. The efficacy analysis included the estimated proportion of eyes with a reduction of 1.00 unit or more in the CCCS relative to baseline (where CCCS baseline value was ≥1.00) or a lack of increase by at least 1 unit (where baseline CCCS <1.00).

For eyes with baseline CCCS ≥1, the response rate was 33% [95% CI: (8, 70)]. For eyes with baseline CCCS <1, the response rate was 89% [95% CI: (52, 100)]. For eyes with baseline CCCS ≥1, mean baseline CCCS score was 1.9 ± 0.6 (mean ± SD) with mean change of -0.5 ± 0.6 at 6 months. For eyes with baseline CCCS <1, mean baseline CCCS score was 0.2 ± 0.1 (mean ± SD) with mean change of 0.1 ± 0.4 at 6 months.

Details on the patient demographics for the three clinical studies are provided in Table 4. Efficacy results from the three clinical studies for treatment of corneal cystine crystal accumulation in patients with cystinosis are summarized in Table 5.

Table 5 : Results of proportion of eyes with corneal cystine crystal score (CCCS) response across Studies 1 to 3

	Study 1		Study 2		Study 3	
STUDY DETAILS						
Number of patients enrolled	247		16		20	
Treatment duration	5.8 ± 5.5 years (Mean ± SD)		1 year		6 months	
Mean age (range)	13.8 years (0.2 – 49.6)		6.5 years (2.7 – 12.0)		13.4 years (5.9 – 27.8)	
PROPORTION OF EYES WITH CORNEAL CYSTINE CRYSTAL SCORE (CCCS) RESPONSE						
	Number of eyes evaluated	Number of responders (%) [95% CI]	Number of eyes evaluated	Number of responders (%) [95% CI]	Number of eyes evaluated	Number of responders (%) [95% CI]
Eyes with Baseline CCCS ≥1.00						
Any Time During Study	291	94 (32%) [27-38]	15	10 (67%) [38-88]	-	NS*
Month 3	-	NS*	14	4 (29%) [8-58]	-	NS
Month 6	-	NS*	14	7 (50%) [23-77]	9	3 (33%) [7-70]
Month 9	-	NS*	14	8 (57%) [29-82]	-	NS*
Month 12	291	27 (9%) [6, 13]	15	7 (47%) [21-73]	-	NS*
Eyes with Baseline CCCS <1.00						
At the end of study	30	4 (13%) [95% CI: (4, 31)]	-	NS	9	8 (89%) [52-100]
*NS = Not Summarized						

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Topical, ocular administration of CYSKLAR is expected to result in low systemic exposure.

General Toxicology

Oral and Intraperitoneal Toxicity Studies

Acute toxicity data are available following systemic administration of cysteamine hydrochloride to rodents. Gastrointestinal ulcers and necrosis of the adrenal gland have been associated with high doses in rats, and depletion of somatostatin was also observed, although the interpretation of these findings in relation to the clinical use are not known.

Ocular Toxicity Studies

Three studies ranging from 3 weeks to 3 months duration were conducted in rabbits where either 0.55% or 0.5% cysteamine HCl eye drop solutions were applied every hour for 8 hours daily. No adverse findings were reported at these concentrations.

Safety Pharmacology

No standard safety pharmacology studies have been performed as these were not considered relevant following topical application.

Genotoxicity

The genotoxic activity of cysteamine has been investigated in *in vitro* studies. Cysteamine was not mutagenic in the Ames test. It produced a negative response in an *in vitro* sister chromatid exchange (SCE) assay in human lymphocytes but a positive response in a similar assay in hamster ovarian cells.

Carcinogenicity

Cysteamine has not been tested for its carcinogenic potential in long-term animal studies.

Reproductive and Developmental Toxicology

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. At an oral dose of 375 mg/kg/day, it reduced the fertility of the adult rats and the survival of their offspring.

Reproductive studies in animals with oral cysteamine were conducted at doses ranging from 37.5 mg/kg/day to 150 mg/kg/day. At doses ≥100 mg/kg/day, teratogenesis were shown. Observed teratogenic findings were intrauterine death, cleft palate, kyphosis, heart ventricular septal defects, microcephaly, exencephaly, and growth deficits. Growth was reduced and mortality increased in rat neonates when mothers received 375 mg/kg/day cysteamine during lactation.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrCYSKLAR™

Cysteamine Ophthalmic Solution

This Patient Medication Information is written for the person who will be taking **CYSKLAR**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have questions about the condition this medication is for or want more information about **CYSKLAR**, talk to a healthcare professional.

What CYSKLAR is used for:

CYSKLAR is used to reduce cystine crystals in the surface of the eye (cornea) in patients with cystinosis.

How CYSKLAR works:

Cystinosis is a rare disease where naturally occurring cystine builds up in body organs and tissues including the surface of the eye (cornea). CYSKLAR changes cystine so that cystine crystals do not build up in the cornea.

The ingredients in CYSKLAR are:

Medicinal ingredients: cysteamine (as cysteamine hydrochloride).

Non-medicinal ingredients: benzalkonium chloride, hydrochloric acid, sodium chloride, sodium hydroxide and water for injection.

CYSKLAR comes in the following dosage forms:

Solution to use as eye drops: 0.44% w/v

Do not use CYSKLAR if:

- you are allergic to cysteamine or to any of the other ingredients of this medicine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CYSKLAR. Talk about any health conditions or problems you may have, including if you:

- are using, have recently used, or might use any other eye drops.
- are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby. It is not known if CYSKLAR will harm your unborn baby.
- wear soft contact lenses.

Other warnings you should know about:

- **Benign Intracranial Hypertension (an increase in pressure inside the skull)**
  - Benign intracranial hypertension has been reported in patients taking oral cysteamine treatment. This has resolved with the use of diuretics (medicines that increase production of urine).
- **Soft Contact Lenses**:
  - You should avoid contact of soft contact lenses with CYSKLAR.

- Soft contact lenses may absorb benzalkonium chloride (a preservative in CYSKLAR). This can cause your contact lenses to become discoloured.
- If you wear soft contact lenses, remove them before using CYSKLAR. Wait at least 15 minutes after using CYSKLAR before putting your contact lenses back in your eyes.

- **Driving and Using Machines:** You may find that your vision is blurred for a few minutes after using CYSKLAR. Do NOT drive or use machines until your vision is clear.

How to take CYSKLAR:

- Use this medicine exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure how to use CYSKLAR.
- Follow the instructions below to use the eye drops.

Step 1: Storing unopened bottles and taking CYSKLAR out of the refrigerator

- Store unopened bottles in the refrigerator in the original carton.
- Each week, remove one new bottle from the refrigerator and open the packaging (carton and foil).

Step 2: Prepare to give yourself CYSKLAR

- Immediately after opening the packaging for the first time, write the date of opening in the space provided on the bottle.
- CYSKLAR can be used for up to 7 days from date of opening. Check the date of opening before giving yourself CYSKLAR.
- Wash your hands thoroughly with soap and water.
- If you wear soft contact lenses:
  - Remove the contact lenses before using CYSKLAR. Do NOT use the drops with soft contact lenses in your eyes.
  - After using CYSKLAR, you should wait 15 minutes before putting contact lenses back in your eyes.

Step 3: Administer CYSKLAR

- The drops should only be used in your eyes.
- Instill one drop of CYSKLAR in each eye, every waking hour.
- Do NOT touch your eyes or surrounding areas with the dropper tip. This may contaminate the solution.
- Tightly close the bottle after use.

Step 4: Storing opened bottle and discarding CYSKLAR

- Once opened, CYSKLAR can be stored at room temperature (20-25°C) for up to 7 days.
- At the end of 1 week (7 days), discard the bottle. There may be medication left in the bottle; however, the bottle must be discarded. The medication can only be used for 1 week after the foil and bottle were opened.

Usual dose:

- Use one drop of CYSKLAR in each eye, every waking hour.

Overdose:

If you put too many drops in your eyes allow a few minutes for blinking of the eyes. If irritation or pain persists, rinse out the eye(s) with an ophthalmic saline or buffered solution. Do not put in anymore drops until it is time for your next regular dose. If pain, irritation and/or eye redness persists please contact your healthcare professional.

If you think you, or a person you are caring for, have taken too much or accidently swallowed CYSKLAR, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

- If you missed a dose of CYSKLAR, you do not need to make up the missed dose. Skip the missed dose and continue with your next scheduled dose.
- Do NOT take two doses at the same time.

Possible side effects from using CYSKLAR:

These are not all the possible side effects you may have when taking CYSKLAR. If you experience any side effects not listed here, tell your healthcare professional.

- Sensitivity to light
- Eye redness
- Eye pain
- Eye irritation
- Headache
- Eye irritation where drops are administered
- Impaired vision (visual fields)

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Common			
Keratitis (inflammation of cornea): eye redness, eye pain, excess tearing, blurred vision, decreased vision, increased sensitivity to light, a feeling that something is in your eye; in presence of keratitis, these symptoms are continual and do not occur just when CYSKLAR are instilled.			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Keep out of reach and sight of children.
- **Before Opening:** Store unopened bottles in the refrigerator at 2°C to 8°C in the intact foil pouch and original carton.
- Open the carton and foil only when starting a new bottle.
- **After Opening:** Record the opening date on the bottle label. During the week of use, store the bottle at room temperature 20°C to 25°C for up to 1 week.
- At the end of 1 week (7 days), discard the bottle. There may be medication left in the bottle; however, the bottle must be discarded because the medication can only be used for 1 week after the foil and bottle were opened.

If you want more information about CYSKLAR:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by calling 1-800-447-0169.

This leaflet was prepared by Leadiant Biosciences, Inc.

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