If you're living with cystinosis, you should know:

THE EYES HAVE IT

cystaran®

(cysteamine ophthalmic solution) 0.44%

In this booklet:

- A brief overview of cystinosis, including genetic etiology, potential complications, and diagnostic criteria
- An exploration of ocular complications of cystinosis, including corneal crystal accumulation and its consequences, and management strategies for physicians
- Information about CYSTARAN® (cysteamine ophthalmic solution) 0.44% for patients with cystinosis

What is CYSTARAN?

CYSTARAN is an eyedrop medication used to treat cystine crystal accumulation in the corneas of patients who have cystinosis.

Please see complete Important Safety Information on page 1 of this brochure or click here for full Prescribing Information.

What is CYSTARAN®?

CYSTARAN is an eyedrop medication used to treat cystine crystal accumulation in the corneas of patients who have cystinosis.

What is the most important safety information I should know about CYSTARAN?

- To help prevent contamination of the dropper tip and eyedrop medication, try to make sure that CYSTARAN is dropped directly onto the eye without touching it. Try not to touch the eyelids or surrounding areas with the dropper tip of the bottle when you are using CYSTARAN. Keep the bottle tightly closed when not in use.
- CYSTARAN contains an ingredient called benzalkonium chloride which can be absorbed by soft contact lenses. Remove contact lenses before using CYSTARAN eyedrops and wait at least 15 minutes before reinserting them.
- CYSTARAN should only be used as an eyedrop medication.

What are the side effects of CYSTARAN?

- The most common side effects of CYSTARAN, which have occurred in at least 10% of people using the medication, were sensitivity to light, eye redness, eye pain and irritation, and headache.

The risk information provided here is not comprehensive. To learn more, talk to your healthcare provider or pharmacist about CYSTARAN. The full FDA-approved product labeling can be found at www.cystaran.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call FDA at 1-800-FDA-1088.

Living with Cystinosis

Cystinosis is a rare but serious multi-system genetic disorder that initially manifests in the kidneys. If cystinosis goes untreated, it can be fatal. Cystinosis is now considered manageable with treatment thanks to the availability of effective medication.

The underlying genetic problem that causes cystinosis (See WHAT CAUSES CYSTINOSIS) affects cells in the entire body, which means that multiple organ systems are at risk from complications—including the eyes. In fact, **cystinosis is a potentially sight-threatening condition** due to disease affecting the retina.

WHAT CAUSES CYSTINOSIS

Cystinosis is caused by a genetic defect in the CTNS gene. This defect is usually a deletion of a specific portion of the gene—the 57-kb segment. However, other types of defects on the CTNS gene or varied levels of deletion exist, and are responsible for how the disease can behave differently in different people.

Functioning CTNS Gene

Defective CTNS Gene

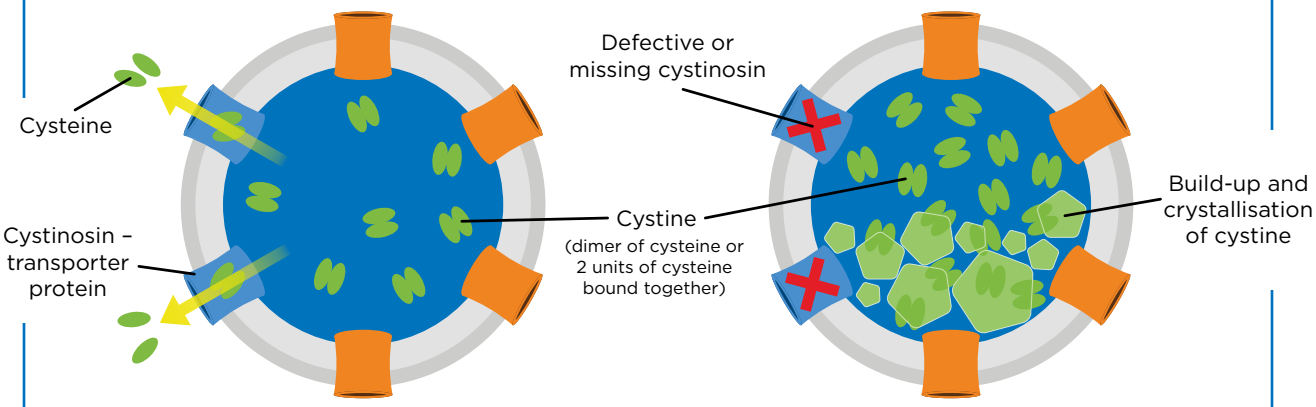
The CTNS gene tells the body how to build an essential transporter protein, cystinosin. If this protein doesn't work, or isn't available in the right amounts, a substance called cystine builds up in cells, eventually forming crystals throughout the body:

Normal Lysosome

In a normal cell, cystinosin helps remove cystine from the cell's lysosome.

Mutated Lysosome

When cystinosin doesn't work properly or isn't present in the right amounts, cystine builds up in the lysosomes of cells throughout the body—including in the eyes

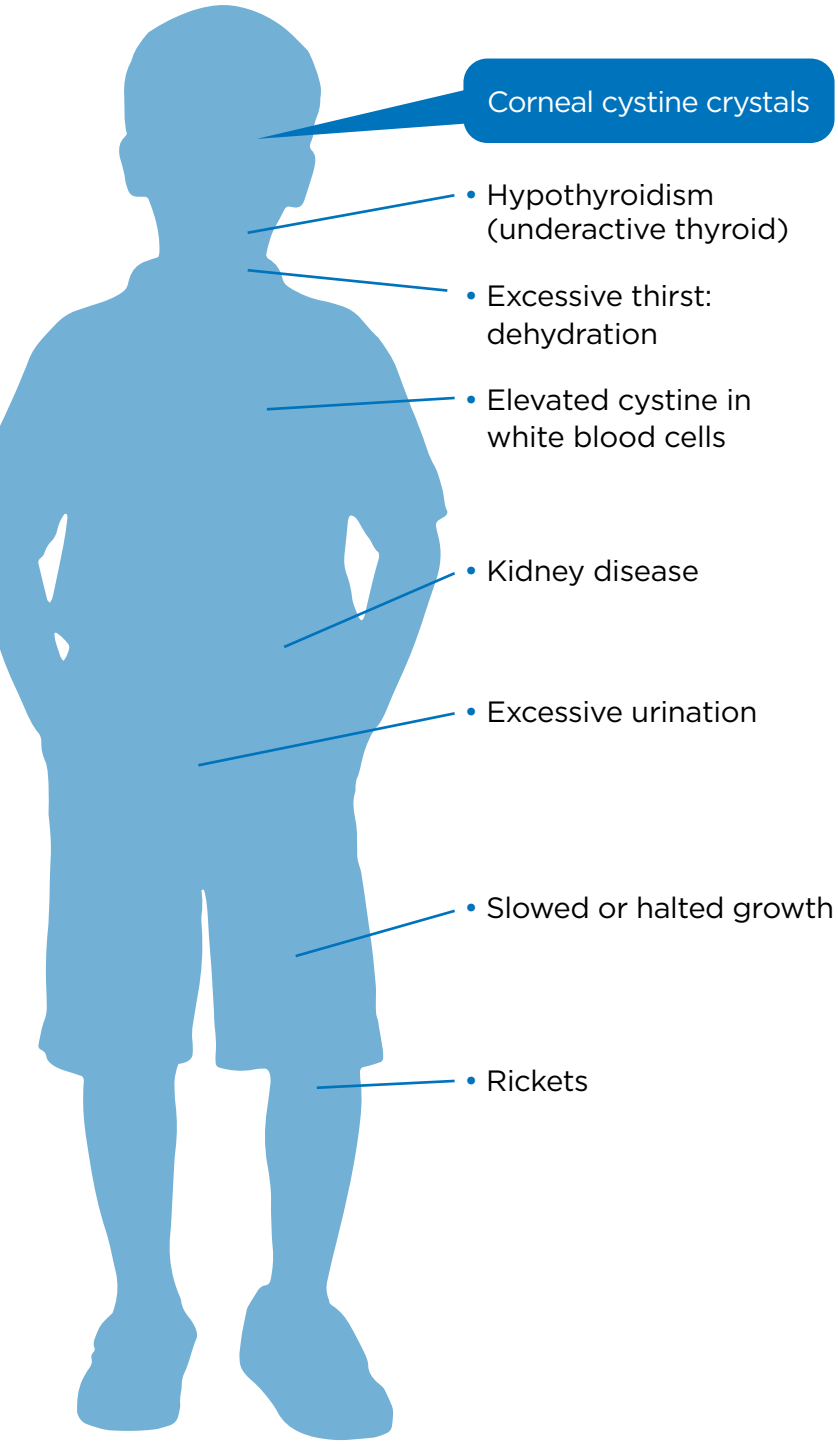


Lysosomes are found inside of cells and contain enzymes which break down molecules into smaller pieces so that they can be recycled for other uses or carried away.

Symptoms of Cystinosis

Cystinosis can affect many different parts of the body. The most common and severe type of cystinosis causes a type of kidney disease (Fanconi's syndrome) during infancy.

EARLY SYMPTOMS OF CYSTINOSIS INCLUDE:



CYSTINOSIS TREATMENT – THEN AND NOW

Before 1960
Life expectancy was short for cystinosis sufferers due to kidney disease

After 1960
Kidney transplants extended lifespans, but showed what other problems can appear due to cystinosis

1976
Research began on cysteamine—a medicine to address cystine crystal buildup in people with cystinosis

1982
Scientists discovered the genetic source of the disease

Late 1980s
Clinical trials for oral cysteamine began. Treatment dramatically increased the lifespan of cystinosis patients

Investigation of eyedrops for eye problems related to cystinosis began, since it was discovered that no blood supply leads to the cornea to deliver oral cysteamine

1994
Oral cysteamine medication was approved by the FDA

2012
CYSTARAN eyedrops were approved by the FDA for treating the accumulation of cystine crystals in the corneas

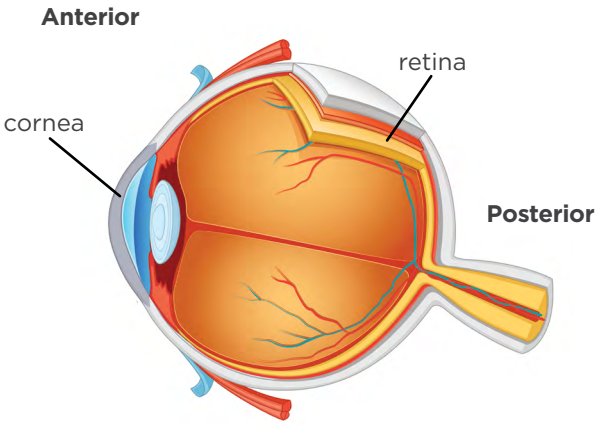
Doctors can detect crystals as early as 16 months in some cystinosis patients. Sensitivity to light from crystal accumulation in the corneas usually starts during late childhood or early adolescence (8-12 years).

Keeping Eyes Healthy with a Cystinosis Diagnosis

If you or a loved one has cystinosis, you should be aware of how the eyes can be affected by crystal accumulation, and what you can do to help support your eye health.

You may already know that cystinosis can impact different parts of the eye, including the retina. Here's something you may not know—oral cystinosis medication may help treat crystals in some parts of the eye, but it can't reach the cornea because there is no blood supply to the cornea to deliver the drug.

HOW CYSTINOSIS AFFECTS THE EYE



Anterior (Front 1/3 of Eye)

When corneal crystals are left to accumulate, they can lead to potentially vision-impairing corneal scarring

Buildup can also lead to chronic red eye, corneal scrapes or injury, inflammation, and even glaucoma

Posterior (Back 2/3 of Eye)

Cystinosis can cause a decrease in the quality and field of vision, night vision, and even perception of colors because of accumulation in the retina

If the retina is damaged enough, significant visual impairment is possible

That means keeping eyes healthy with a cystinosis diagnosis can't just be a matter of taking your oral medication as directed. To fight corneal crystal accumulation, you also need a therapy that goes directly on the eye, such as an eyedrop.

EYE CARE IS FOR **ALL AGES**

Very young children can have a high level of crystal buildup, which doctors can detect as early as 6 months in some patients and after 16 months in all patients.

Children and adolescents may feel foreign body sensation (like something is in the eye) as well as sensitivity to light, which can cause eye pain and difficulty opening the eyes in daylight.

It's never too late to start using an eyedrop therapy, since patients of all ages can reduce their crystal buildup with proper treatment.

If the disease goes too far without treatment or care, scarring can result that can be painful or even affect vision. Eye surgery may be required.

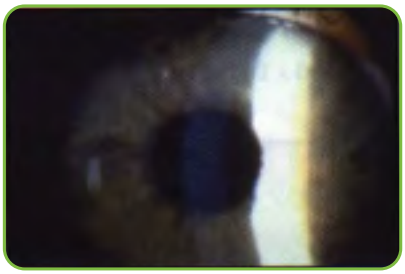
WHAT TO EXPECT AT AN EYE EXAM

The initial test for corneal crystals will probably involve a **slit lamp microscope**, which is a microscope with a bright light that's used with most eye exams.

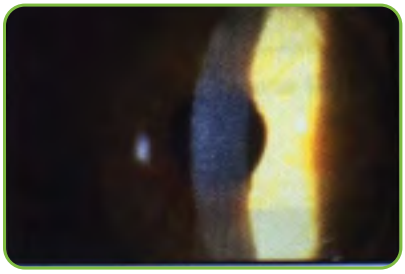
The slit lamp microscope can show whether you have crystals in your corneas and help the ophthalmologist give an estimate of how densely they are packed. They may use a **CCCS** to describe how many crystals are present, which stands for **corneal cystine crystal score**. A CCCS goes from 0 (no crystals) to 3 (heavily packed with crystals) in increments of 0.25.

Here are some examples of eyes with corneal crystals as seen through a slit lamp microscope, along with their CCCS numbers:

CCCS = 0.00



CCCS = 1.00



CCCS = 2.00

CCCS = 3.00

See how the eyes with higher CCCS scores appear cloudy? Those are corneal cystine crystals.

START THE CONVERSATION

Here are some questions you can ask the physicians:

Nephrologist (Kidney Doctor)

- What are some strategies for taking medications for cystinosis properly?
- How often should cystinosis patients follow up with you about their health?
- Can you refer me to an ophthalmologist with expertise?

Ophthalmologist (Eye Doctor)

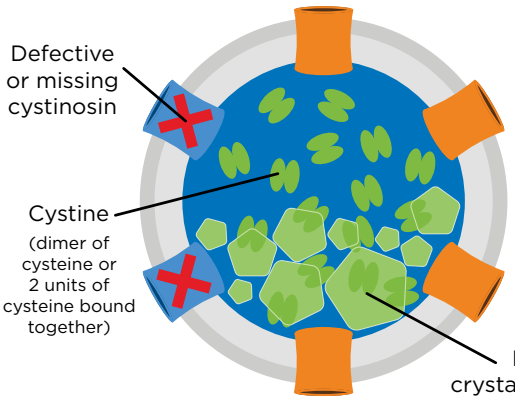
- What are some ways to keep eyes healthy with a cystinosis diagnosis?
- How often should cystinosis patients follow up with you about their eye health?
- What symptoms should cystinosis patients watch out for? / Are there any eye symptoms that you should be told about right away?
- What tools do you use to detect crystals in the corneas?
- If crystals are detected, what options are there for treating the eyes?
- Can you walk me through the best way to apply eye drops?
- If it's necessary to take eye drop medication in a public place or a classroom, what are best practices for keeping the medication from being contaminated and keeping eyes safe?
- Can patients who use contact lenses take eye drop medications like CYSTARAN?
- How frequently should I take CYSTARAN?

A Treatment for Corneal Crystal Accumulation Due to Cystinosis—CYSTARAN

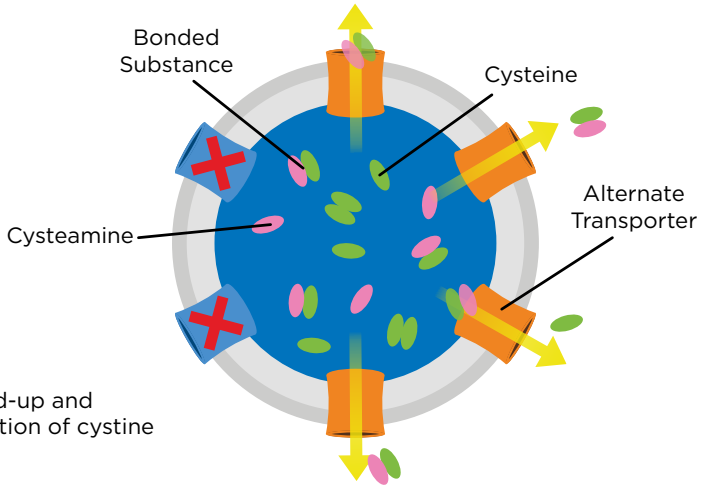
HERE'S HOW CYSTARAN WORKS:

- Cysteamine, the active ingredient in CYSTARAN, works to help decrease the accumulation of cystine crystals in the body's tissues.
- Cysteamine binds to and changes cystine. The bound substance can be removed from the lysosomes of the body's cells without a need for cystinosin and is not harmful to the eye.

Lysosome Affected by Cystinosis

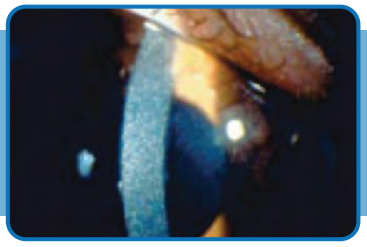
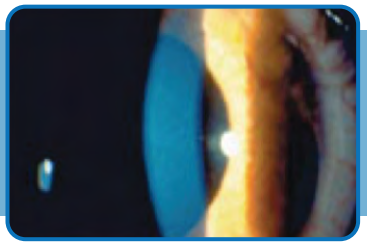
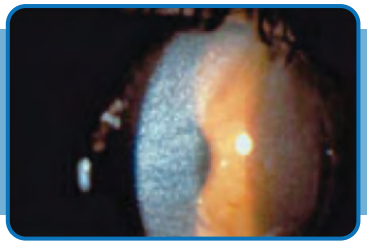
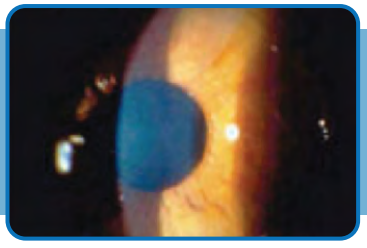


After Taking Cysteamine



The use of CYSTARAN has been demonstrated to be effective at reducing corneal crystals

SEE EXAMPLES OF TREATMENT WITH CYSTARAN®*

Age at Start of Treatment:	BEFORE	After 15 Months of Treatment
5-year-old patient		
	BEFORE	**After 12 Months of Treatment**
25-year-old patient		

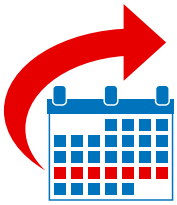
**Corneal slit-lamp photographs of patients treated with CYSTARAN. These examples represent patients who responded to treatment and in subsequent follow up appointments. Duration of therapy varied from 8 – 41 months. Response may vary from patient to patient.*

How to Take CYSTARAN

ALWAYS WASH YOUR HANDS THOROUGHLY WITH SOAP AND WATER BEFORE ADMINISTERING EYE DROPS.

Instill one drop of CYSTARAN in each eye, **every waking hour**

Do not touch dropper tip to any surface, as this may contaminate the solution



Discard after 1 week of use

There may be medication left in the bottle; however, the bottle must be discarded by the patient because the **medication is only stable for 1 week after thawing**

HOW TO STORE CYSTARAN

- Store bottles in the freezer in the original carton.
- Each week, remove one new bottle from the freezer.
- Allow the bottle to thaw completely (approximately 24 hours) prior to use.
- After the bottle is completely thawed, record the discard date on the bottle label. The discard date is seven (7) days from the day the bottle is thawed.
- Store the thawed bottle at no greater than room temperature for up to 1 week. No refrigeration required after thawing. Do no refreeze the bottle.
- Remember to discard the bottle at the end of 1 week (7 days). There may be medication left in the bottle; however, you must discard it because the medication is only stable for 1 week after thawing.

CYSTARAN IS ONLY AVAILABLE FROM ALLIANCERX WALGREENS PHARMACY

Your medication will be shipped directly to your home.

To order, call 1-877-534-9627

Friendly associates exclusively available to help CYSTARAN patients will be happy to assist you Mon–Fri, 8AM–7PM EST.

Want to learn more about supporting eye health with **CYSTARAN?** Visit **www.cystaran.com**

cystaran®
(cysteamine ophthalmic solution) 0.44%

Summary of Information about CYSTARAN® (cysteamine ophthalmic solution) 0.44%

What is CYSTARAN used for?

CYSTARAN is an eyedrop medication used to treat cystine crystal accumulation in the corneas of patients who have cystinosis.

What warnings should I know about CYSTARAN?

To help prevent contamination of the dropper tip and eyedrop medication, try to make sure that CYSTARAN is dropped directly onto the eye without touching it. Try not to touch the eyelids or surrounding areas with the dropper tip of the bottle when you are using CYSTARAN. Keep the bottle tightly closed when not in use.

CYSTARAN contains an ingredient called benzalkonium chloride which can be absorbed by soft contact lenses. Remove contact lenses before using CYSTARAN eyedrops and wait at least 15 minutes before reinserting them.

CYSTARAN should only be used as an eyedrop medication.

What are the side effects of CYSTARAN?

In at least 10% of patients, CYSTARAN causes sensitivity to light, eye redness, eye pain and irritation, and headache.

How do I take CYSTARAN?

Once every waking hour, instill one drop of CYSTARAN into each eye. Do not let the CYSTARAN dropper tip touch your eyelid or the surrounding area.

How do I store CYSTARAN?

1. Store CYSTARAN bottles in the freezer in the original carton.
2. Each week, remove one new bottle from the freezer.
3. Allow the bottle to thaw completely (about 24 hours) before using.
4. After the bottle is thawed, record the discard date on the bottle label. The discard date is 7 days (1 week) from the day the bottle is thawed.
5. Store the thawed bottle at no greater than room temperature for up to 1 week. No refrigeration required after thawing. **Do not refreeze the bottle.**
6. At the end of 1 week, throw away the entire bottle even if there is still medication inside. The medication is only stable for 1 week after thawing.

The risk information provided here is not comprehensive. To learn more, talk to your healthcare provider or pharmacist about CYSTARAN. The full FDA-approved product labeling can be found at www.cystaran.com.

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Leadiant Biosciences