Discover Cystinosis

(sis-tin-oh-sis)

This brochure has been developed by Chiesi and is intended for people living with cystinosis, either as parents or carers.

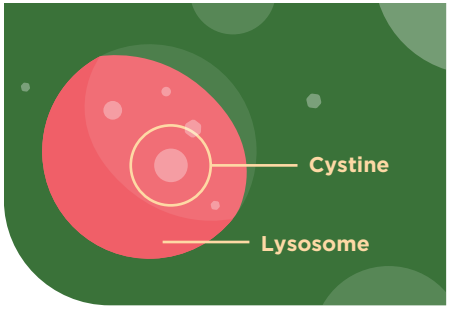
Chiesi
global rare diseases

What is cystinosis?

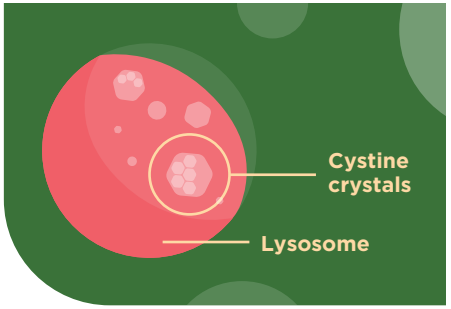
Cystinosis is an extremely rare genetic condition[1] which affects fewer than 2 people in every million.[2]

The symptoms of cystinosis usually appear before a child turns one year old. Cystinosis runs in families. The disease is hereditary, resulting from genes inherited from the parents. Cystinosis is caused by a gene that carries a mutation. A gene with a mutation has lost its normal structure and function. In people with cystinosis, the genetic mutation prevents the movement of an amino acid called cystine out of the body's cells. When cystine cannot move out of the cells, it builds up to abnormally high levels.[1,3]

Person without cystinosis[2]



Person with cystinosis[2]

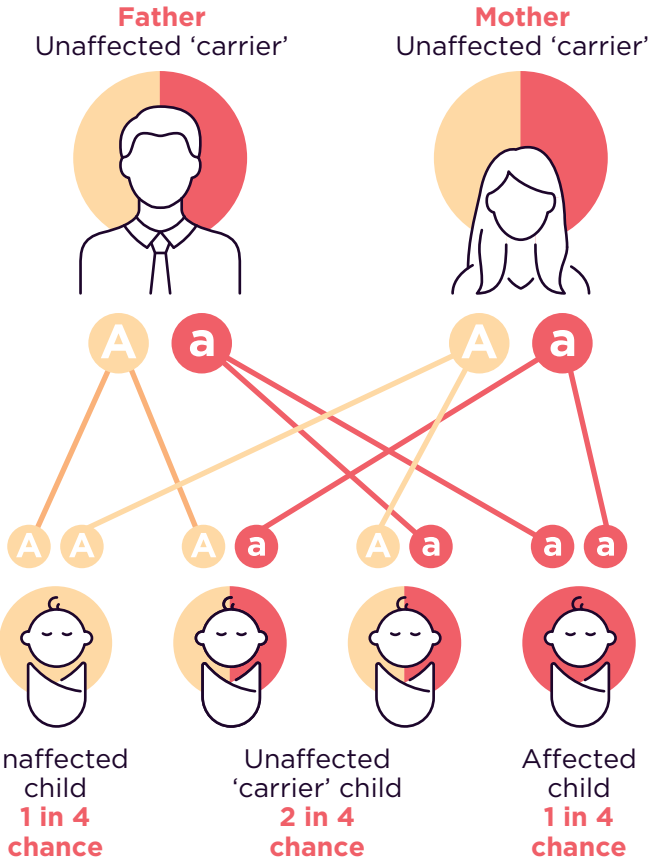


When cystine builds up, it forms crystals within cells that can cause long-term damage to the organs, including kidneys, eyes, liver, muscles, pancreas, and brain.[1,3]

This damage cannot be reversed, but it can be delayed or reduced.[1]

How is cystinosis passed down?

Cystinosis is an inherited disease passed from parents to child. Cystinosis can only develop in children who receive a non-working copy of the cystinosis gene from each parent.[1]



What are the different types of cystinosis a person might have?

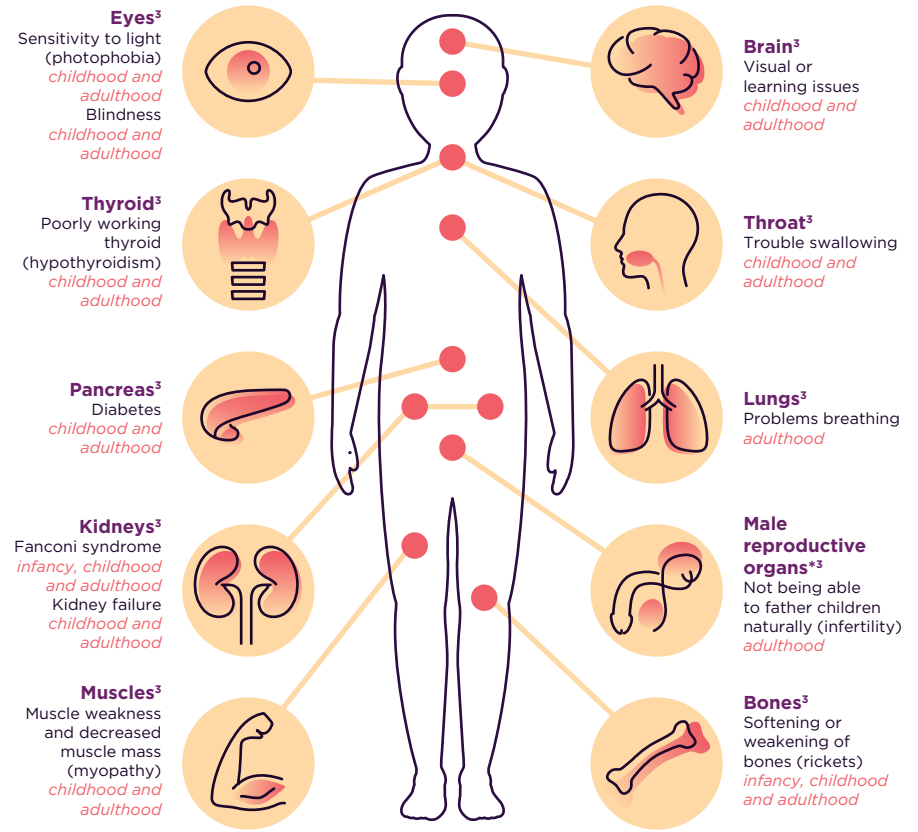
There are three types of cystinosis, classified by how much the kidneys are affected and how old the person is when symptoms start appearing:[1]

- **Infantile nephropathic cystinosis[1]**
  95% of people with cystinosis have this type. Kidney problems start to appear between 6 and 12 months of age, and if the disease is not treated, patients develop end stage renal disease by around 10 years old.
- **Juvenile, or late-onset, nephropathic cystinosis[1,3]**
  Only 5% of people with cystinosis have this type. It's typically diagnosed between childhood and late adolescence and tends to progress much more slowly than the other types.
- **Adult, or ocular, cystinosis[1]**
  Very rare; diagnosed in adults. This form usually affects the eyes, but not the kidneys or other organs. The effects on the eyes may not typically appear until adulthood or middle age.

How does cystinosis affect the body?

Because nephropathic cystinosis affects every cell in the body, its symptoms are very broad and diverse. Although the kidneys are affected first, almost every organ in the body is at risk of damage.[3]

Patients with nephropathic cystinosis appear normal at birth, but within the first year of life they often present signs that suggest their kidneys are not working as well as they should.[1,3]



*Cystinosis has not been shown to cause infertility in women. If you are pregnant, planning on becoming pregnant, or breastfeeding, talk with your doctors about which treatments might be right for you.[1,3]

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How does cystinosis change over time?

As people with nephropathic cystinosis get older, the accumulation of cystine in all cells leads to a range of possible symptoms that affect different parts of the body.[3]

Continuous, lifelong cystine accumulation potentially damages all organs and tissues,[3,5] resulting in severe complications.[3,5,6]

Progression of disease over time[3,5]
Timeline shows age of onset of complications in patients not receiving cystine-depleting therapy.

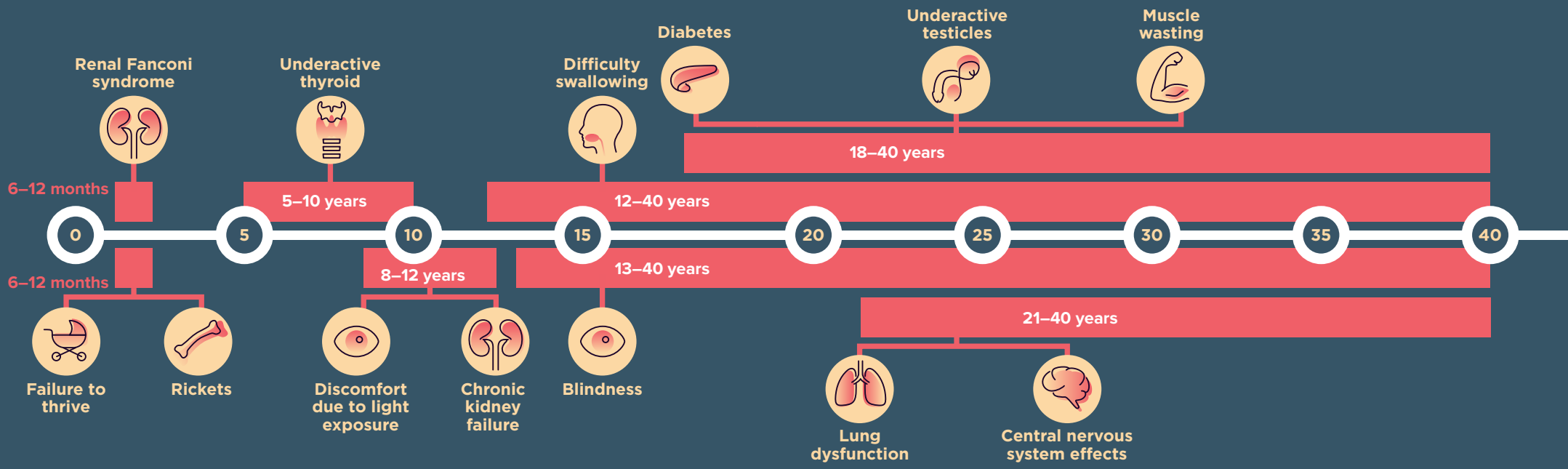


Figure adapted from Nesterova G and Gahl WA. Pediatr Nephrol 2013[5] and Gahl WA, et al. N Engl J Med 2002.[3]

What is Fanconi syndrome?

Over time, nephropathic cystinosis causes damage to the kidneys.[3]

This damage makes the kidneys increasingly unable to absorb essential nutrients and filter out the body's waste – a disorder known as Fanconi syndrome.[3]

In people with Fanconi syndrome, nutrients that would normally be absorbed instead are passed through the kidneys and eliminated through pee (urine).[3]

Fanconi syndrome symptoms include:

- Excessive thirst and peeing (urination)[1,7]
- Reduced appetite[8]
- Weight loss[8]
- Slow growth[7]
- Softening or weakening of bones (rickets)[1,7]

Although kidneys are the first organs to be affected by increased cystine levels, other organs are also affected over time.[3] Kidney problems can get worse throughout childhood and possibly reach a stage where they fail to work, in this case dialysis is used before kidney transplant.[3] Cystinosis can continue to progress in other organs even after renal transplantation.[3]

How is cystinosis diagnosed?

- Cystinosis can be diagnosed using a test that looks at the levels of cystine in the white blood cells. White blood cells are used because they are a well-known place of cystine accumulation and are easy to obtain via a blood test. If there is a high level of cystine in these cells, the diagnosis of cystinosis can be confirmed.[1]
- A slit-lamp examination for eye crystals which appear by 1–2 years of age.[8] This examination may be the initial criterion for diagnosing late-onset patients.[8]
- If available, genetic testing for *CTNS* mutations confirms the diagnosis and characterises the specific mutations[5] and also detects cystinosis in unborn babies (antenatal screening in at-risk pregnancies).[1,8]

It's important that a diagnosis of cystinosis is made as soon as possible. This helps the patient get prompt treatment to prevent long-term complications.[7]

Cystinosis should be suspected in children who show signs of renal Fanconi syndrome and don't gain weight as they should (failure to thrive), experience growth retardation (short stature and poor weight gain are common), or show signs of loss of appetite or rickets.[8]

What are the goals for cystinosis treatment?

- The **main goal of cystinosis treatment** is to delay disease progression. Without treatment, high levels of cystine can damage your kidneys, eyes, muscles, and many other organs.[3,9,10]
- Consistent adherence to cystine-depleting therapy maintains growth and delays renal and extra-renal complications.[9,11]
- To stay healthy, cystine-depleting therapy should be started as soon as cystinosis is diagnosed and should continue life-long as recommended by the doctor.[3,8,10,12]
- It is important not to postpone or miss a dose, as missing a dose of even a few hours can increase cystine levels.[13] Therapy to reduce cystine should be continued even after kidney transplantation.[3]

Monitoring cystinosis

People with cystinosis need several examinations to monitor their condition throughout their life. As patients grow from childhood, through adolescence, to adulthood, their healthcare needs will change. Transitioning from paediatric to adult care is particularly challenging and requires a strong supportive network between patients, carers, support specialists and physicians.[2]

White blood cell cystine test

People with cystinosis should have the levels of cystine in the white blood cells checked regularly by their physicians:[14]

- 2 weeks after starting treatment until dose adjustments are completed[14]
- Every 3 months to help settle on the best dose[14]

With treatment, the aim is to keep the levels of cystine low.[3,14]

The monitoring for people with cystinosis at different stages of life:[2,8,14,17]

Infants/children	
White blood cell cystine test	Every 3 months
Kidneys	Every 3 months
Growth and nutrition	Every 3 months
Brain	
Eyes	Every year
Adolescents	
White blood cell cystine test	Every 3 months
Eyes	Every year
How well they treatment regimen is followed (adherence)	
Symptoms throughout the body	
Kidneys	
Hormones	Examinations to identify when puberty starts
Preparing for transition to adult care	Begins in mid-adolescence
Adults	
White blood cell cystine test	Every 3 months
Symptoms throughout the body	
Eyes	Every year
How well they treatment regimen is followed (adherence)	
Kidneys	
Hormones	

What should you expect when living with cystinosis?

HCPs involved in treatment

Cystinosis can affect many organs throughout the body, so patients, parents or carers may need support for their emotional and physical well-being.[16] Throughout the patient's life, different teams of specialists are involved. These typically include:[2,17,16]

- kidney specialists (nephrologists)
- hormone specialists (endocrinologists)
- brain specialists (neurologists)
- eye specialists (ophthalmologists)
- gut specialists (gastroenterologists)
- dietitians
- physical and behavioural therapists

Supportive treatments for people with cystinosis[3,8,8,14,17]

Kidneys
Fluid and salt replacement. Treatment which reduces swelling/inflammation to lower kidney filtration and reduce the amount of urine produced.[3]

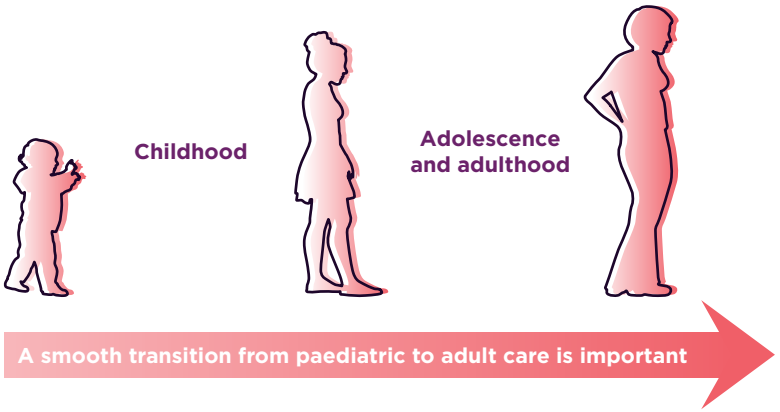
Treatment to reduce the amount of protein in the urine.[3]

Diet and nutrition
A surgeon may place a tube known as a gastrotomy or G-tube, through the stomach, to feed the child.[8] Nutrients may be given by injection into a vein, known as total parenteral nutrition. Phosphate and vitamin D can be given for rickets.[6,8]

Hormones
Hormones may be offered for patients of short stature.[3,8] Thyroid hormone or testosterone replacement may be needed.[3,8]

Other therapies
Treatments to reduce levels of cystine can delay damage to the kidneys, improve growth, and delay late complications of cystinosis.[14,17] However, cystine-depleting therapy alone cannot fully treat the symptoms of cystinosis.[17]

The HCPs who treat cystinosis change as the patient gets older[2,8]



Paediatric care is usually led by:

Paediatric Nephrologist

Often makes the initial diagnosis and usually coordinates medical care through adolescence.

Adult care is usually led by:

Adult Nephrologist

May assume the primary role in coordinating care at the appropriate time for the patient's transition from paediatric to adult care.

The HCPs who treat cystinosis change as the patient gets older[2,8]

Multidisciplinary patient management

Different healthcare teams for patients with cystinosis[5,6,18]

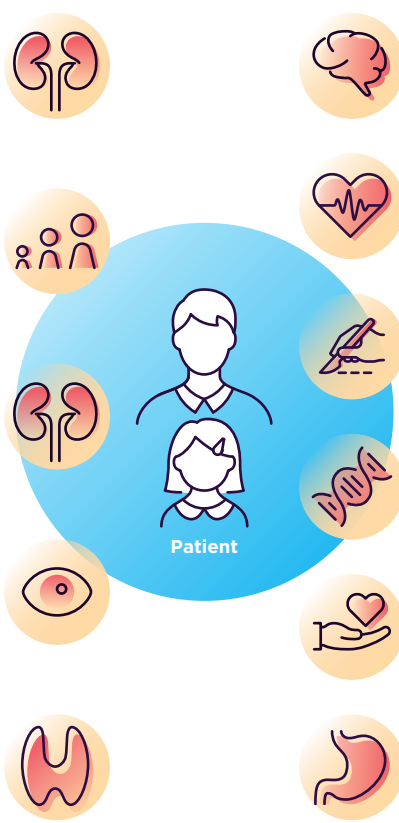
Adult nephrologist[7,8]
May assume the primary role in coordinating care at the appropriate time for the patient's transition from paediatric to adult care

Other specialists[8,18]
Provide additional services that many patients with cystinosis may require such as nutrition counselling, occupational therapy, speech therapy, behavioural nursing care, and medication management and instruction

Paediatric nephrologist[7,8]
Often makes the initial diagnosis and usually coordinates medical care through adolescence

Ophthalmolgist[7,8]
Monitors vision and eye health and treats ophthalmic complications

Endocrinologist[8]
Evaluates the need for growth hormone therapy, treats hypothyroidism and diabetes mellitus



Neurologist[8]
Addresses neuromuscular problems, including swallowing difficulties due to myopathy, which generally appear in late adolescence

Cardiologist[8]
Evaluates cardiovascular risk and treats heart

Transplant surgeon[8,18]
Provides medical care before and after a transplantation. He/she also performs the kidney transplantation

Human geneticist[7,8,18]
Confirms a cystinosis diagnosis through genetic tests and conducts genetic consultation and prenatal diagnostic tests

Paediatrician/ internist[18]
Provides general medical care

Gastroenterologist[18]
Manages gastrointestinal issues

Cystinosis affects different organ systems and requires the collaborative efforts of a range of medical specialists to optimise clinical outcomes.[16]

Therapeutic options

At present, there is no cure for the condition, and to date, management of cystinosis has largely focused on treatment of the various symptoms that can be present. Currently the only target-specific treatment for nephropathic cystinosis is cystine-depleting therapy, drugs that have been shown to reduce cystine levels in cells throughout the body. Cystine-depleting eyedrops are used to dissolve cystine crystals in the eyes.[3,6] Treatment for cystinosis should be started as early in life as possible and will need to continue throughout life, even after a kidney transplant.[3,7]

The goal of cystine-depleting therapy is to delay or prevent damage to cells by keeping cystine levels low at all times.

When the level of cystine-depleting therapy in the body of a person with nephropathic cystinosis is not sufficient, the amount of cystine in the cells quickly rises to unsafe levels. Because of this, skipping or delaying a dose of cystine-depleting therapy can create the risk of damage to the body and allows cystine levels to rise. That's why it's so important to keep cystine levels controlled all the time by taking cystine-depleting therapy exactly as the doctor recommends.[11,13]

This is a serious challenge for adolescents and young adults as they come to adulthood after transition from paediatric to adult care.[7]

Kidney transplant is an effective treatment for the kidney failure in patients with cystinosis.[19]

There are lots of websites you can go to for help and support

There's a supportive community out there that's eager to provide information, understanding and advice. A host of organisations and support groups is just a few clicks away.

International patient organisations

Cystinosis Foundation (USA)

Cystinosis Research Network (USA)

Cystinosis Network Europe (CNE)

References:

1. Elmonem MA et al. *Orphanet J Rare Dis* 2016;11:47.
2. Langman CB et al. *Kidney Int* 2016;89:1192–1203.
3. Gahl WA et al. *N Engl J Med* 2002;347(2):111–121.
4. Darr A et al. *J Community Genet* 2016;7:65–69.
5. Nesterova G & Gahl WA. *Pediatr Nephrol* 2013;28(1):512–519.
6. Nesterova G and Gahl W. *Pediatr Nephrol* 2008;23(6):863–878.
7. Emma F et al. *Nephrol Dial Transplant* 2014;29:iv87–94.
8. Wilmer MJ et al. *Pediatr Nephrol* 2011;26(2):205–215.
9. Gahl WA et al. *Ann Intern Med* 2007;147:242–250.
10. Brodin-Sartorius A et al. *Kidney Int* 2012;81:179–189.
11. Gahl WA et al. *N Engl J Med* 1987;316:971–997.
12. Markello TC et al. *N Engl J Med* 1993;328(16):1157–1162.
13. Levtchenko EN et al. *Pediatr Nephrol* 2006;21(1):110–113.
14. European Medicines Agency, PROCYSBI (cysteamine) Summary of Product Characteristics.
15. Ariceta G et al. *Nefrología (English Edition)* 2015;35(3):304–321.
16. Nesterova G. and Gahl WA. Infantile nephropathic cystinosis standards of care: a reference for people with infantile nephropathic cystinosis, their families, and medical team. Cystinosis Research Foundation, 2012. Available at https://cystinosis.org/wp-content/uploads/2019/01/CRN_StandardsOfCare_FINAL-1.pdf.
17. Cherqui S. Kidney Int. 2012;81(2):127–129.
18. Cystinosis Research Network. Available at https://cystinosis.org/images/research/article-library/overview/Cystinosis-Parent-Handbook-Final.pdf.
19. Kleta R et al. *Pediatr Nephrol* 2005:20(4):452–454.

Date of preparation: March 2022.
ALL_22_113

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