FOR CAREGIVERS

Meet Cora,
a real CRYSVITA
patient

The power to treat XLH at its source

Effect intended for illustration. Healing of rickets was assessed at week 40 in pediatric patients.

CRYSVITA® targets the underlying cause of X-linked hypophosphatemia (XLH)

What is CRYSVITA?

CRYSVITA (burosumab) is a prescription medicine used to treat adults and children 6 months of age and older with X-linked hypophosphatemia (XLH).

Important Safety Information

You should not take CRYSVITA if:

- You take an oral phosphate supplement and/or a specific form of vitamin D supplement (such as calcitriol, paricalcitol, doxercalciferol, calcifediol).
- Your phosphorus levels from a blood sample are within or above the normal range for age.
- You have kidney problems.

Please see Important Safety Information throughout this brochure and full Prescribing Information for CRYSVITA in pocket.

CRYSVITA®
burosumab-twza
Injection 10, 20, 30 mg/mL

What is XLH?

XLH is lifelong and progressive

X-linked hypophosphatemia (XLH) is a genetic condition (something people are born with) that can change over time. It can impact both children and adults.

What causes XLH?

People with XLH have lower than normal levels of phosphorus in their blood. This is caused by a change (variant) in the *PHEX* gene. This variant causes the body to produce too much of a hormone called fibroblast growth factor 23 (FGF23).

Meet Cora, a real CRYSVITA patient

XLH causes the body to lose phosphorus by this process:

The body produces too much FGF23

Extra FGF23 causes the body to lose too much phosphorus through the urine instead of keeping it in the bloodstream

Low phosphorus levels can lead to weakened bones

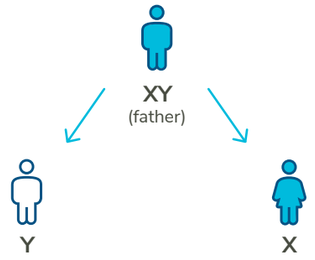
This process is known as phosphorus wasting. Low levels of phosphorus in the blood are known as hypophosphatemia (the H in XLH).

Low phosphorus levels can continue to affect your child's bones and muscles as they age.

XLH can be inherited from parents

The X and L in XLH stand for X-linked, meaning the condition is passed down through the X chromosome. Chromosomes are structures inside the body's cells that contain your genes. Everyone has at least one X chromosome. Men have an X and a Y chromosome (XY), and women have two X chromosomes (XX).

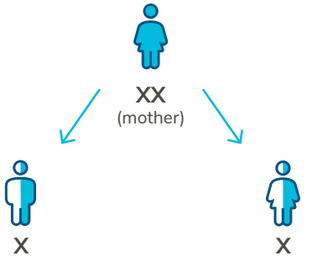
If a father has XLH:



0% chance of son developing XLH

100% chance of daughter developing XLH

If a mother has XLH:



50% chance of son developing XLH

50% chance of daughter developing XLH

XLH can also happen spontaneously

XLH can also occur in those without any family history. This is known as a spontaneous case of XLH. Up to 3 in 10 people with XLH develop it due to spontaneous gene variants, which can then be passed on to their future children.

XLH symptoms can start early in life

In children, XLH can cause:

- Weakening of growing bones (rickets)
- Delayed growth
- Short stature

XLH symptoms can vary from person to person. Be sure to tell your child's doctor how XLH is affecting them.

How CRYSVITA® works

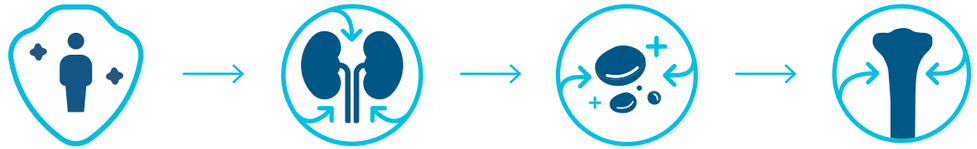
What is CRYSVITA?

CRYSVITA is the first and only FDA-approved treatment for adults and children 6 months of age or older living with XLH.

How CRYSVITA impacts phosphorus

CRYSVITA works by targeting the underlying cause of XLH (too much FGF23) to help the body keep more of the phosphorus it needs.

CRYSVITA helps restore the balance of phosphorus in the body



CRYSVITA blocks FGF23

By keeping FGF23 activity in check, the kidneys can better reabsorb phosphorus

Phosphorus levels in the blood increase

Phosphorus can then be deposited into the bones

Watch a video about how CRYSVITA works

Important Safety Information

What is the most important information you should know about CRYSVITA?

- Some patients developed allergic reactions (e.g., rash and hives) while taking CRYSVITA. Your doctor will monitor you for symptoms of an allergic reaction while you are taking CRYSVITA. Your treatment may need to be discontinued for serious allergic reactions.
- High levels of phosphorus in the blood have been reported in some patients taking CRYSVITA. This may be related to a risk of high calcium levels in the kidneys. Your doctor will collect blood samples to monitor your levels. If you are already taking CRYSVITA, dose interruption and/or dose reduction may be required based on your serum phosphorus levels.

How CRYSVITA was studied

The benefits and safety of CRYSVITA treatment were studied in children with XLH.

STUDY 1

NUMBER OF CHILDREN

29 on CRYSVITA

32 on conventional therapy

AGES

1-12 years old

LENGTH OF TREATMENT

64 weeks

This study (Study 1) compared the effects of CRYSVITA with the effects of oral phosphate and active vitamin D (calcitriol or alfacalcidol). In the study, these supplements were referred to as “conventional therapy.”

CRYSVITA was also assessed in 2 other studies in children. See full results from the studies

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CRYSVITA®
burosumab-twza
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CRYSVITA® was effective in treating children with XLH

Rickets

Children on CRYSVITA had **improved healing of rickets** at week 40. The average Radiographic Global Impression of Change (RGI-C) score[a] was 1.9 in patients on CRYSVITA and 0.8 in patients on conventional therapy.

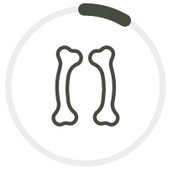
Also, more children on CRYSVITA **had substantial healing of their rickets**[a] compared with conventional therapy at week 40.

CRYSVITA

72%

21 out of 29 patients

VS



Conventional therapy

6%

2 out of 32 patients

These results were maintained at week 64. On average, children receiving CRYSVITA had a greater improvement in lower extremity skeletal abnormalities than patients receiving conventional therapy at week 64.

Children on CRYSVITA **had a greater reduction in the severity of their rickets**[b] compared with conventional therapy at week 64.[c]

CRYSVITA

70%

reduction in severity

VS

Conventional therapy

32%

reduction in severity

[a] RGI-C is a scale from -3 (severe worsening of rickets) to +3 (complete or near-complete healing of rickets) used to measure the change in rickets. An RGI-C score of ≥+2.0 means substantial healing of rickets.

[b] Thacher Rickets Severity Score (RSS) was used to assess XLH-related rickets. This is a 10-point scale from 0 (no rickets) to 10 (severe rickets) used to measure the severity of rickets. A lower RSS score means an improvement in rickets severity.

[c] The average change in RSS at week 40 was -2.0 in children on CRYSVITA compared with -0.7 for those on conventional therapy. At week 64, the average change was -2.2 in the CRYSVITA group compared with -1.0 for conventional therapy. The average RSS at baseline was 3.2 in both groups.

Important Safety Information

What is the most important information you should know about CRYSVITA? (cont'd)

- Administration of CRYSVITA may result in reactions at the injection site, such as hives, reddening of the skin, rash, swelling, bruising, pain, severe itching of the skin, and collection of blood outside of a blood vessel (i.e., hematoma). Call your doctor if you develop an injection site reaction. CRYSVITA may be discontinued if severe injection site reactions occur.

Phosphorus levels

Children on CRYSVITA **had increased average levels of phosphorus** in the blood compared with conventional therapy from the start of the study to week 64.

CRYSVITA

2.4 mg/dL WEEK 0 → **3.3** mg/dL WEEK 64

VS

Conventional therapy

2.3 mg/dL WEEK 0 → **2.5** mg/dL WEEK 64

Height

Children on CRYSVITA **had a greater average increase in height compared** with conventional therapy (at 64 weeks).

CRYSVITA

+0.17

Average change in height z-score

VS

Conventional therapy

+0.02

Average change in height z-score

The height z-score measures how close a child's height is to the average height of all children of the same age and sex.

Important Safety Information

What are the possible side effects of CRYSVITA?

- Adverse reactions that were seen in children with XLH are:
  - Fever
  - Injection site reaction
  - Cough
  - Vomiting
  - Pain in arms and legs
  - Headache
  - Tooth abscess
  - Dental cavities
  - Diarrhea
  - Decreased vitamin D levels
  - Toothache
  - Constipation
  - Muscle pain
  - Rash
  - Dizziness
  - Nausea

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Safety was also studied in CRYSVITA®

The following side effects were observed in 10% or more of children who were treated with CRYSVITA[d]:

- Fever
- Injection site reaction
- Cough
- Vomiting
- Pain in arms and legs
- Headache
- Tooth abscess
- Dental cavities
- Diarrhea
- Decreased vitamin D levels
- Constipation
- Rash
- Nausea

These are not all the possible side effects of CRYSVITA. Talk to your child's doctor for medical advice about side effects.

[d]More children in the CRYSVITA group experienced these reactions versus the conventional therapy group.

Meet Cora,
a real CRYSVITA patient

Important Safety Information

What are the possible side effects of CRYSVITA? (cont'd)

- Adverse reactions that were seen in adults with XLH are:
  - Back pain
  - Headache
  - Tooth infection
  - Restless legs syndrome
  - Decreased vitamin D levels
  - Dizziness
  - Constipation
  - Muscle spasms
  - Phosphorus levels increased in the blood

CRYSVITA dosing

1 dose every 2 weeks

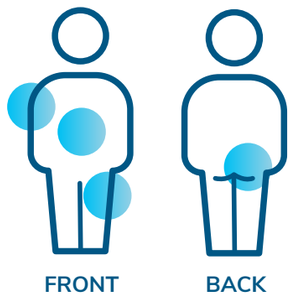
The dosage (the amount of CRYSVITA your child takes) is based on body weight and will be determined by their doctor. **Adjustments to your child's dosage may be necessary if their weight changes during treatment.** In some cases, more than 1 injection may be required.

While taking CRYSVITA, tell your doctor if your child experiences:

- An allergic reaction such as rash or hives
- A rash, swelling, bruising, or other reaction at the injection site
- New or worsening restless legs syndrome

CRYSVITA is given as an injection by a healthcare provider

This type of injection is called a subcutaneous injection, which means it is given by a needle into tissue just below the skin. The needle should not touch your child's nerves, muscles, or bones.



Your child will get their injection in **1 of 4 places**. Each time, the injection spot will be switched to a different one.

- Upper arms
- Upper thighs
- Buttocks
- Stomach

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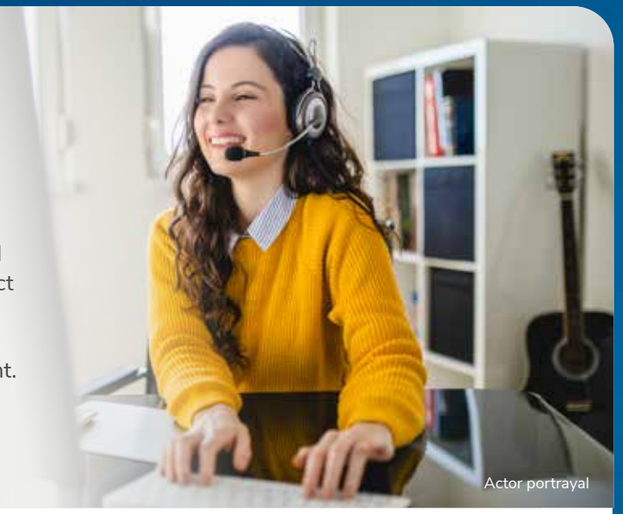
Getting started on CRYSVITA®



Kyowa Kirin Cares can help

Kyowa Kirin Cares is a program with dedicated specialists and case managers who can connect patients and caregivers to the support they need—from access and reimbursement assistance to ongoing support during treatment.

Before enrolling in Kyowa Kirin Cares

For your child to be prescribed CRYSVITA, you may need to provide their insurance company with information such as:

- Genetic test results that confirm your child's XLH diagnosis
- Family history of XLH
- Medical history of symptoms and treatment

Talk to your child's doctor about enrolling in Kyowa Kirin Cares

After enrolling, your child's dedicated case manager can help you by:

- Sharing details about your financial assistance options
- Answering general questions about CRYSVITA
- Helping you and your child stay on track with treatment
- Providing educational tools and resources
- Calling routinely to check in and offer support

Important Safety Information

What are the possible side effects of CRYSVITA? (cont'd)

- Narrowing of the spaces within the spine is common in adults with XLH, and pressure on the spinal cord has been reported in adults taking CRYSVITA. It is not known if taking CRYSVITA worsens the narrowing of the spaces within the spine or the pressure on the spinal cord.

Kyowa Kirin Cares Co-pay Assistance Program

$0 out-of-pocket cost

Patients may pay as little as $0 for CRYSVITA.

95% of the eligible, commercially insured patients who were enrolled in the Kyowa Kirin Cares Co-pay Assistance Program had $0 out-of-pocket costs for CRYSVITA.[e]

Additional Kyowa Kirin Cares financial assistance options for CRYSVITA may be available to patients who qualify. Ask a Kyowa Kirin Cares case manager for more information.

Call 833-KK-CARES (833-552-2737) Monday through Friday, 8 AM to 8 PM (ET), to speak with a Kyowa Kirin Cares case manager about financial assistance options.

[e]**Kyowa Kirin Cares Co-Pay Assistance Program Terms and Conditions**
Patients who are enrolled in any federal or state healthcare program, including, without limitation, Medicaid, Managed Medicaid, Medicare, Medicare Advantage, Medigap, CHAMPVA, TriCare, Veterans Affairs (VA), or Department of Defense (DoD), or any state or patient assistance program are not eligible for Kyowa Kirin Cares Co-Pay Assistance Program. The Kyowa Kirin Cares Co-Pay Assistance Program for CRYSVITA helps commercially insured individuals who are residents of the United States (including the United States territories) and who are prescribed CRYSVITA for a use approved by the Food and Drug Administration (FDA) pay for their eligible out-of-pocket costs and cost-sharing for CRYSVITA and the associated cost-sharing for drug administration, up to a specified maximum benefit per calendar year. To learn the maximum benefit of financial assistance available to you under the Kyowa Kirin Cares Co-Pay Assistance Program, call Kyowa Kirin Cares at 833-KK-CARES (833-552-2737). Either the patient, or the patient's legal guardian or representative, must personally enroll in the Kyowa Kirin Cares Co-Pay Assistance Program. Health insurance plans, pharmacy benefit managers, employers, payors, or any of their representatives or agents are prohibited from enrolling patients or assisting patients with enrolling in the Kyowa Kirin Cares Co-Pay Assistance Program.

Note that individuals residing in Massachusetts or Rhode Island (or elsewhere as prohibited by law) may not be eligible for financial assistance related to the administration/injection of CRYSVITA. In order to be eligible for the Program, individuals must provide a signed authorization compliant with the Health Insurance Portability and Accountability Act of 1996 and the regulations thereunder (collectively "HIPAA"). The Program does not cover the costs of physician office visits or evaluations, blood work or other testing, or transportation or other related services. Individuals may not seek reimbursement from any health savings, flexible savings, or other healthcare reimbursement account for any amounts received from the Co-Pay Assistance Program. Claims accrued 90 days prior to enrollment in Kyowa Kirin Cares will not be eligible for Co-Pay Assistance. **The Program is NOT insurance.** Void if copied, transferred, purchased, altered, or traded, and where prohibited and restricted by law. For additional terms and conditions, call Kyowa Kirin Cares at 833-KK-CARES (833-552-2737).

Terms and Conditions are subject to change at any time without prior notification. Kyowa Kirin reserves the right to make eligibility determinations, to set parameters for its Programs, to monitor participation, and to change, modify, or discontinue its Programs at any time without notice.

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Staying on CRYSVITA®

XLH is a progressive disease with symptoms that vary from person to person

Low phosphorus levels can continue to impact your child's bones and muscles over time. That's why it is important that they keep going to their appointments and stick to their CRYSVITA dosing schedule as prescribed.

Set treatment goals

Setting goals can be an important part of your child's treatment journey. Talk with your doctor about how to create a plan for setting treatment goals.

Plan for life's changes

Your child's Kyowa Kirin Cares case manager can help you figure out coverage for life changes such as:

- Moving to a new town
- Going to college
- Changing insurance providers

Need help finding a doctor who treats XLH?

Use this HCP Finder to locate a doctor near you.

Important Safety Information

Before taking CRYSVITA, tell your doctor about all of your medications (including supplements) and medical conditions, including if you:

- Are taking oral phosphate and/or active vitamin D (such as calcitriol, paricalcitol, doxercalciferol, calcifediol).
- Are pregnant, think you may be pregnant, or plan to become pregnant. There is not enough experience to know if CRYSVITA may harm your unborn baby. Report pregnancies to the Kyowa Kirin, Inc. Adverse Event reporting line at 1-844-768-3544.
- Are breastfeeding or plan to breastfeed. There is not enough experience to know if CRYSVITA passes into your breast milk. Talk with your doctor about the best way to feed your baby while you receive CRYSVITA.

Get ready to talk with your child's doctor about CRYSVITA

Early diagnosis and treatment are important

When it comes to treating XLH, your child's doctor needs all the information they can get. When you talk with your child's doctor, be sure to paint a clear picture of their symptoms and their impact. That way, you can have a better conversation about CRYSVITA and whether it is right for your child.

Meet Cora, a real CRYSVITA patient, and her mother

Important Safety Information

While taking CRYSVITA, tell your doctor if you experience:

- An allergic reaction such as rash or hives
- A rash, swelling, bruising, or other reaction at the injection site
- New or worsening restless legs syndrome

These are not all the possible side effects of CRYSVITA. Call your doctor for medical advice about side effects.

You may report side effects to the FDA at (800) FDA-1088 or **www.fda.gov/medwatch**. You may also report side effects to Kyowa Kirin, Inc. at 1-844-768-3544.

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Discover the **power**

CRYSVITA® is the only FDA-approved treatment for XLH that targets the underlying cause of the disease

Get started today:

- Talk with your child's doctor about CRYSVITA to see if it could be right for them
- Enroll in the Kyowa Kirin Cares program and start getting support for your child's treatment journey
- Ask a Kyowa Kirin Cares case manager about ways to help with the cost of CRYSVITA

Effect intended for illustration. Healing of rickets was assessed at week 40 in pediatric patients.

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KYOWA KIRIN

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