FOR PATIENTS

The power to treat XLH at its source

Meet Aly,
a real CRYSVITA patient

Effect intended for illustration. Healing of fractures was assessed at week 24 and improvement in weak or soft bone was assessed at week 48 in adult 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.

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 you 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).

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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

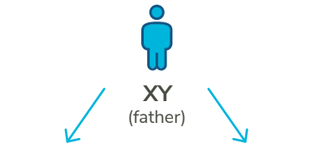
This process is known as phosphorus wasting. Low levels of phosphorus in the blood are known as hypophosphatemia (the H in XLH).

Low phosphorus levels can continue to affect your bones and muscles as you age.

XLH can be inherited from your 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 your 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).

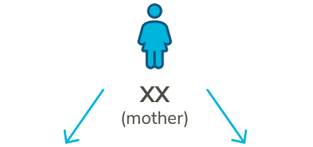
If a father has XLH:



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 change over time

In addition to symptoms that can appear early in life, adults may experience:

- Soft or weakened bone (osteomalacia)
- Broken bones (fractures) and areas of weakened bone that are not completely broken (pseudofractures)
- Joint stiffness

XLH symptoms can vary from person to person. Be sure to tell your doctor how XLH is affecting you.

How CRYSVITA® works

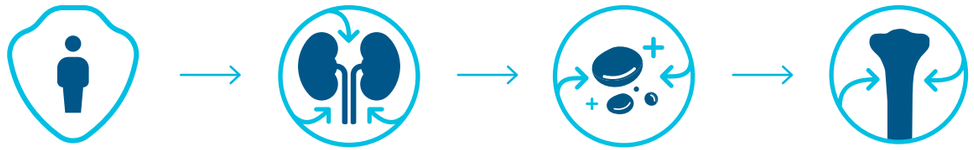
What is CRYSVITA?

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

How CRYSVITA was studied

Doctors looked at the risks and benefits of treatment with CRYSVITA in 148 adults with XLH in 2 studies.

STUDY 4

Number of people:
134

Ages:
19 to 66 years old

Length of treatment:
48 weeks

- Doctors compared treatment with CRYSVITA to placebo[a]
- 68 adults were given CRYSVITA and 66 adults were given placebo once every 4 weeks for the first 24 weeks
- After 24 weeks, adults who had been taking placebo were switched to CRYSVITA for the last 24 weeks of the study

[a]Placebo is a treatment that does not contain the medicine being tested.

STUDY 5

Number of people:
14

Ages:
25 to 52 years old

Length of treatment:
48 weeks

- Small samples of bone (bone biopsies) were taken from 14 adults with XLH and looked at for signs of soft or weakened bone (osteomalacia)
- Bone samples were taken before the patients started treatment with CRYSVITA and again after they took CRYSVITA once every 4 weeks for 48 weeks

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.

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

CRYSVITA® was effective in treating adults with XLH

Phosphorus levels (Study 4)

More people on CRYSVITA saw their **phosphorus levels increase** to within the normal range[b] compared with those who took placebo between the start of the study and week 24.

94%
CRYSVITA
64 out of 68 patients had normal phosphorus levels

vs

8%
Placebo[c]
5 out of 66 patients had normal phosphorus levels

[b]Normal levels of phosphorus in the blood for this group of patients was defined as a range of 2.5 to 4.5 milligrams/deciliter (mg/dL). The normal range of phosphorus varies by age and sex.

Fractures and pseudofractures (Study 4)

People on CRYSVITA showed **healing of more fractures and pseudofractures** compared with placebo between the start of the study and week 24.

43%
CRYSVITA
28 out of 65 fractures and pseudofractures healed

vs

8%
Placebo[c]
7 out of 91 fractures and pseudofractures healed

From weeks 24 to 48, patients who kept taking CRYSVITA showed continued healing. Patients who switched to CRYSVITA from placebo also showed healing (46% of fractures and 33% of pseudofractures healed at week 48).

[c]Placebo is a treatment that does not contain the medicine being tested.

Important Safety Information

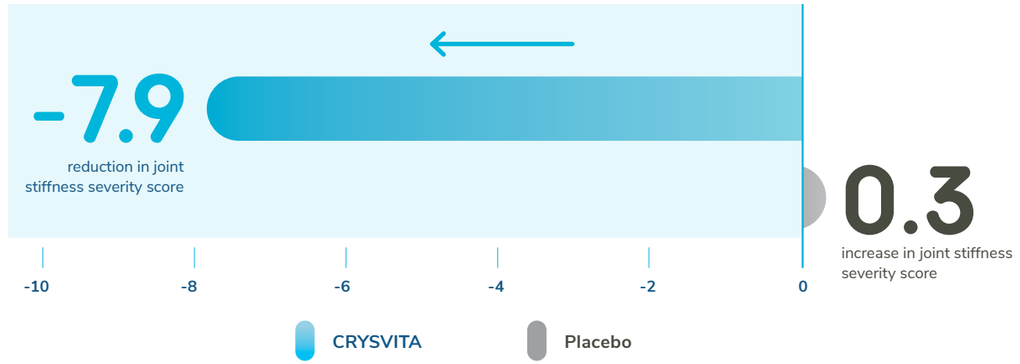
What is the most important information you should know about CRYSVITA? (cont'd)

- 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.

Joint stiffness (Study 4)

People on CRYSVITA reported an **improvement in joint stiffness** compared with those on placebo between the start of the study and week 24, where lower scores reflect symptom improvement. Patients did not report a difference between CRYSVITA and placebo for pain intensity or physical activity.

Average change in joint stiffness severity score after 24 weeks[d]



[d]In Study 4, stiffness was measured using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) patient questionnaire. The stiffness severity score ranges from 0 to 100. Lower scores mean less severe symptoms.

Osteomalacia (Study 5)

People on CRYSVITA showed **improved bone hardening** (bone mineralization) after 48 weeks.

57%
CRYSVITA
reduction in (unmineralized) soft bone[e]

[e]Their bone tests showed a decrease in the amount of soft, unmineralized bone compared to the total bone, which is measured by the osteoid volume to bone volume ratio.

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®

In Study 4, the most common side effects observed in more than 5% of adults treated with CRYSVITA were[†]:

- Back pain
- Headache
- Tooth infection
- Restless legs syndrome
- Decreased vitamin D levels
- Dizziness
- Muscle spasms
- Constipation
- Phosphorus levels increased in the blood

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.

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

[†]These reactions occurred in more than 5% of patients in the CRYSVITA group and in at least 2 patients more than with placebo.

See the full results from the studies

Meet Aly,
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 4 weeks

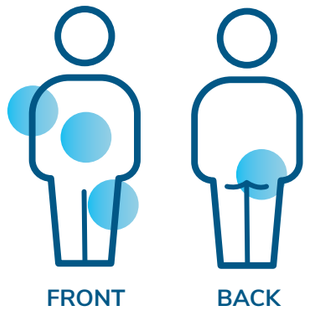
The dosage (the amount of CRYSVITA you take) is based on body weight and will be determined by your doctor. **Adjustments to your dosage may be necessary if your weight changes during treatment.** In some cases, more than 1 injection may be required.

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

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 nerves, muscles, or bones.



You will get your 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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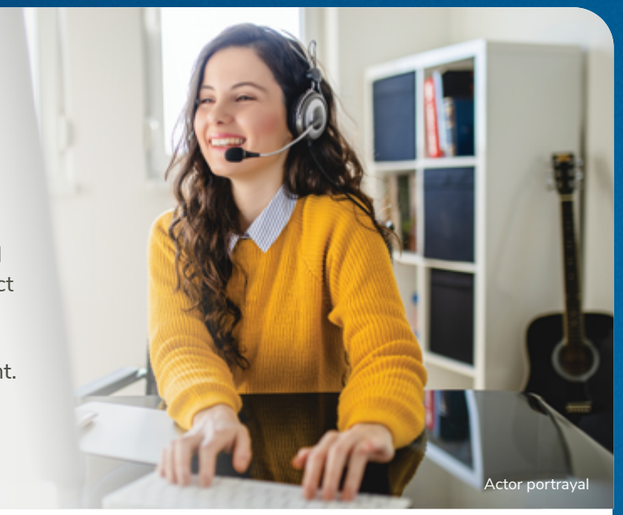
Getting started on CRYSVITA®


Actor portrayal

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

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

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

Talk to your doctor about enrolling in Kyowa Kirin Cares

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

- Sharing details about your financial assistance options
- Answering general questions about CRYSVITA
- Helping you stay on track with your treatments
- 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.[9]

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.

[9]**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® can help make a difference

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

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

Set treatment goals

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

Plan for life's changes

Your Kyowa Kirin Cares case manager can help you figure out your 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 Specialist 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 doctor about CRYSVITA

Early diagnosis and treatment are important

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

Meet Aly,
a real CRYSVITA patient

Important Safety Information

While taking CRYSVITA, tell your doctor if you experience:

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- 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

Meet Aly, a real CRYSVITA patient

Get started today:

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

Effect intended for illustration. Healing of fractures was assessed at week 24 and improvement in weak or soft bone was assessed at week 48 in adult patients.

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- 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.
- 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.

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

Visit CRYSVITA.com to learn more

KYOWA KIRIN

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