A TARGETED APPROACH TO LOW PHOSPHORUS IN TIO

Discover CRYSVITA, a prescription medicine used to treat adults and children 2 years of age and older with fibroblast growth factor 23 (FGF23)–related hypophosphatemia in tumor-induced osteomalacia (TIO) when the tumor cannot be located or removed.

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.

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

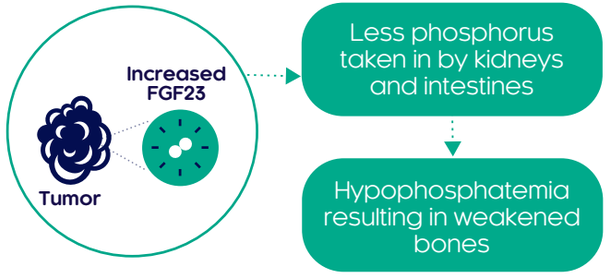
Please see Important Safety Information on pages 8-9 and throughout this brochure and attached full Prescribing Information.

What is TIO?

TIO is a disorder that causes low levels of **phosphorus** in the blood, resulting in weak bones.

TIO is caused by tumors that produce a protein called **fibroblast growth factor 23 (FGF23)**.

- This means that there is too much FGF23 in the body, which causes phosphorus to be lost through the urine and reduces the body's ability to activate **vitamin D**
- This leads to low levels of phosphorus circulating in the bloodstream, which is also called **hypophosphatemia**
- These low levels of phosphorus lead to **osteomalacia**, which weakens bones and makes them prone to break easily



Important terms to know

Phosphorus: Second most abundant mineral in the body that contributes to healthy bones and teeth.

FGF23: A protein that regulates phosphorus and vitamin D in the body.

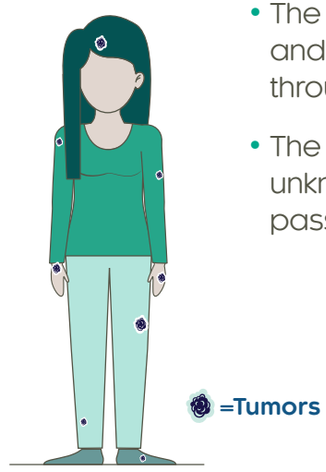
Vitamin D: A nutrient used by the body to maintain strong bones.

Hypophosphatemia: Low levels of phosphorus in the blood.

Osteomalacia: Weakening and softening of the bones.

What causes TIO?

The tumors that cause TIO are most often found in the hands, feet, arms, and legs but can also be anywhere in the body.



- The slow-growing tumors are frequently very small, and they may be difficult or impossible to find through scans ordered by your doctor
- The cause of the tumors that lead to TIO is unknown, and there is no evidence that TIO is passed down through family members

What are the symptoms of TIO?

Hypophosphatemia from TIO can cause symptoms including:

Bone pain

Weakening of the bones (osteomalacia)

These symptoms can be so severe that some people with TIO may be wheelchair-bound or bedridden.

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Is misdiagnosis common in TIO?

95% of TIO patients get misdiagnosed

It can take many years from the start of symptoms to receive an accurate diagnosis of TIO.

Misdiagnosis is common. In many instances people are diagnosed with osteoporosis, inflammatory arthritis, or fibromyalgia because these conditions can have similar symptoms.

Can tumors be removed to help with TIO symptoms?

Tumors responsible for TIO can sometimes be found and removed through surgery. This can bring back the levels of phosphorus and vitamin D in the body. But this isn't always possible. Because of their size, tumors can be hard to find and remove.

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

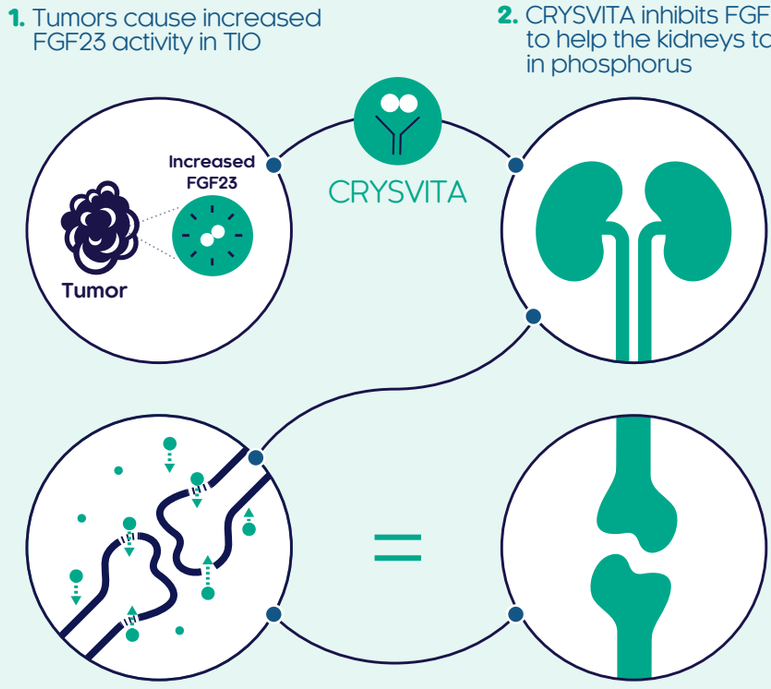
- Some patients developed allergic reactions (e.g., rash and hives) while taking CRYSVITA. Your doctor will monitor you for symptoms of an allergic reaction while you are taking CRYSVITA.
- High levels of phosphorus in the blood have been reported in some patients taking CRYSVITA. This may be related to a risk of high calcium levels in the kidneys. Your doctor will collect blood samples to monitor your levels.
- If you undergo treatment of the underlying tumor, your dose should be interrupted and adjusted to prevent high levels of phosphate.
- 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).

What is CRYSVITA?

CRYSVITA is a medication approved by the FDA to help treat the symptoms of TIO by targeting the underlying cause of FGF23-related hypophosphatemia.

How does CRYSVITA work?

CRYSVITA is an antibody that helps block the activity of FGF23 to restore the balance of phosphorus and vitamin D in the body.



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How can CRYSVITA help?

CRYSVITA may help with the symptoms of TIO by:

Increasing serum phosphorus levels to a normal range

Healing osteomalacia

How was CRYSVITA studied?

The benefits and risks of CRYSVITA have been tested in 2 clinical studies of 27 adults with TIO.

STUDY 6

Total adults: 14 | **Ages:** 33 to 68 years | **Treatment length:** 144 weeks

STUDY 7

Total adults: 13 | **Ages:** 41 to 73 years | **Treatment length:** 88 weeks

What are the possible side effects of CRYSVITA?

- Adverse reactions that were seen in adults with TIO are:
  - Tooth infection
  - Muscle spasms
  - Dizziness
  - Constipation
  - Injection site reaction
  - Rash
  - Headache

What results were seen in clinical studies with CRYSVITA?

In Study 6 and 7

Increased phosphorus levels in the blood

100% (27/27) of patients achieved an increase in serum phosphorus levels throughout the studies

In Study 6 and 7

Helped heal osteomalacia (softened bones)

34% improvement in bone mineralization at week 48, showing healing of osteomalacia in Study 6 (n=9). Similar results were seen in Study 7 (n=3)

- Bone scans suggest healing of bone abnormalities at weeks 48 through 144 in Study 6

Ask your doctor if CRYSVITA may be right for you or your child

Talk to your doctor if you have any questions or concerns about taking CRYSVITA and managing your treatment plan.

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  - Constipation
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  - Rash
  - Headache

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 1-888-756-8657.
- 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.

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 **1-888-756-8657.**

Please see attached full Prescribing Information for additional Important Safety Information.

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How is CRYSVITA administered?

CRYSVITA is an injection that your healthcare provider will administer.

For adults, your doctor will start with CRYSVITA every 4 weeks

For children, your doctor will start with CRYSVITA every 2 weeks

After initial treatment, your doctor may adjust how much and how often CRYSVITA is given.

What can I expect at my CRYSVITA appointment?

Starting any new medication may take some time to get used to. Before receiving CRYSVITA, your healthcare provider will take a blood sample to measure your serum phosphorus levels. Once treatment begins, they will continue to check serum phosphorus levels and may adjust your CRYSVITA dosage as needed.

- CRYSVITA will be administered by your doctor (or another healthcare provider)

- Talk to your UltraCare Guide to see if home injection may be an option and if it is covered by your insurance

- After the injection, you will be monitored for a short period of time
- Talk to your doctor if you have questions about the injection process

What questions should I ask my doctor about CRYSVITA?

- What is CRYSVITA?
- What are the possible benefits of starting treatment?
- How will this treatment affect the symptoms of my TIO?
- What are the possible side effects of CRYSVITA?

Preparing for your appointment

To make the most of your appointment and to make sure your doctor has all the information needed for your treatment, remember to:

- ✔ Bring copies of any relevant medical records
- ✔ Have your medical history ready to share with your doctor
- ✔ Bring a list of any medications or treatments you currently take
- ✔ Write down any other questions you have for your doctor

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Receive patient assistance to access CRYSVITA with UltraCare®

UltraCare®

Ultragenyx is committed to patients with rare diseases, which is why we created UltraCare, a suite of services designed to help you access CRYSVITA.

Our UltraCare Guides are experienced professionals who are passionate about supporting you at every step. They can help you:

- ✔ Understand your insurance coverage and explain your benefits
- ✔ Determine your eligibility for financial and patient assistance programs
- ✔ Access patient support resources

To learn more, visit UltraCareSupport.com or contact our UltraCare Guides at 1-888-756-8657; option 1.

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To learn more about CRYSVITA, talk to your doctor today or visit CRYSVITA.com.

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