We are providing this for your health benefit. You may want to bring this overview with you to educate others who are not familiar with XLH or CRYSVITA.

FOR X-LINKED HYPOPHOSPHATEMIA

DISCOVER CRYSVITA® (BUROSUMAB-TWZA)

What is CRYSVITA?

CRYSVITA® is the first and only FDA-approved therapy for the treatment of XLH in patients more than one year of age. CRYSVITA is designed to bind to and inhibit excess FGF23 in patients with XLH.[1]

CRYSVITA is a subcutaneous injection administered by a healthcare provider. Children with XLH receive CRYSVITA every two weeks. Adults with XLH receive CRYSVITA every four weeks.

What is XLH?[2-5]

- X-linked hypophosphatemia (XLH) is a rare skeletal disorder that affects both children and adults.
- People with XLH produce too much of a protein called fibroblast growth factor 23 (FGF23).
- FGF23 controls the balance of phosphorus in the blood.
- Too much FGF23 causes phosphate wasting or loss of phosphorus through the urine.

Signs and Symptoms of XLH

In children, XLH causes rickets, which leads to delayed growth and short stature. In adults, XLH causes osteomalacia (softening of the bones). Osteomalacia puts them at increased risk of bone fractures.[1-3]

XLH Inheritance

XLH is inherited in families, making family history an important diagnostic consideration.[3,5] Other family members who show similar signs and symptoms should speak to a doctor. XLH is X-linked, which means if a mother has XLH, all of her children have a 50% chance of inheriting the condition. If a father has XLH, all of his daughters and none of his sons will inherit XLH.

One-third (1/3) of XLH cases are **spontaneous** and appear in people with no family history.

CONTRAINDICATIONS[1]

- Do not use CRYSVITA with oral phosphate and active vitamin D analogs.
- Do not initiate CRYSVITA if serum phosphorus is within or above the normal range for age.
- CRYSVITA is contraindicated in patients with severe renal impairment or end stage renal disease.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity

- Discontinue CRYSVITA if serious hypersensitivity reactions occur and initiate appropriate medical treatment

Hyperphosphatemia and Risk of Nephrocalcinosis

- For patients already taking CRYSVITA, dose interruption and/or dose reduction may be required based on a patient's serum phosphorus levels.

Injection Site Reactions

- Discontinue CRYSVITA if severe injection site reactions occur and administer appropriate medical treatment.

Please see back page for additional Important Safety Information and enclosed full Prescribing Information.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Pediatric Patients

- The most common adverse reactions (more than 10%) in pediatric XLH patients are: headache, injection site reaction, vomiting, pyrexia, pain in extremity, vitamin D decreased, rash, toothache, myalgia, tooth abscess, and dizziness.

Adult Patients

- The most common adverse reactions (more than 5% and in at least 2 patients more than placebo) in adult XLH patients are: back pain, headache, tooth infection, restless leg syndrome, vitamin D decreased, dizziness, constipation, blood phosphorus increased.
- Spinal stenosis is prevalent in adults with XLH and spinal cord compression has been reported. It is unknown if CRYSVITA therapy exacerbates spinal stenosis or spinal cord compression.

USE IN SPECIFIC POPULATIONS

- There are no available data on CRYSVITA use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Serum phosphorus levels should be monitored throughout pregnancy. Report pregnancies to the Ultragenyx Adverse Event reporting line at **1-888-756-8657**.
- There is no information regarding the presence of CRYSVITA in human milk, or the effects of CRYSVITA on milk production or the breastfed infant.

PATIENT COUNSELING INFORMATION

- Instruct patients to contact their physician if hypersensitivity reactions, injection site reactions, and restless leg syndrome induction or worsening of symptoms occur.

You may report side effects to the FDA at **(800) FDA-1088** or **www.fda.gov/medwatch**. You may also report side effects to Ultragenyx at **1-888-756-8657**.

Please see enclosed full Prescribing Information for a complete discussion of the risks associated with CRYSVITA.

References

1. CRYSVITA® (burosumab-twza) Prescribing Information. April 2018. **2.** Carpenter TO, Imel EA, Holm IA, Jan de Beur SM, Insogna KL. A clinician's guide to X-linked hypophosphatemia. *J Bone Miner Res.* 2011;26:1381-8. **3.** Ruppe MD. X-linked hypophosphatemia. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews®* [Internet]. Seattle, University of Washington, Seattle; 1993-2017. **4.** Linglart A, Biosse-Duplan M, Briot K, et al. Therapeutic management of hypophosphatemic rickets from infancy to adulthood. *Endocr Connect.* 2014;3(1):R13-30. **5.** Gaucher C, Walrant-Debray O, Nguyen TM, Esterle L, Garabedian M, Jehan F. PHEX analysis in 118 pedigrees reveals new genetic clues in hypophosphatemic rickets. *Hum Genet.* 2009;125:401-11.

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