Endorsed by the **American Society for Bone and Mineral Research (ASBMR)** and the **Endocrine Society**[1,a]

New International Working Group clinical practice guidelines for managing **XLH in adults**

Access the full publication

Developed by a panel of 43 global experts in X-linked hypophosphatemia (XLH), along with a patient partner and methodology experts[1]

Guidelines were based on an expert survey, a narrative review, and 2 systematic reviews comparing (1) the impact of burosumab (CRYSVITA®) versus conventional therapy (active vitamin D and phosphate salts) or no therapy, and (2) the impact of conventional therapy versus no therapy on patient-important outcomes.[1]

Treatment recommendations (GRADEd)[1]

CRYSVITA is:

✓ **Recommended**

over no therapy in adults with fractures or pseudofractures

(***strong recommendation,*** *moderate certainty*)

CRYSVITA is:

✓ **Suggested**

over no therapy in adults without fractures or pseudofractures

(***conditional recommendation,*** *low certainty*)

CRYSVITA is:

✓ **Suggested**

over conventional therapy in adults with fractures or pseudofractures

(***conditional recommendation,*** *low certainty*)

Indication: CRYSVITA® (burosumab-twza) is a fibroblast growth factor 23 (FGF23) blocking antibody indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.

Panel recognizes there may be limitations to drug therapy accessibility.[1] See the publication for full GRADEd and non-GRADEd guidelines, including complete methodology, assessment, monitoring, and further treatment insights.

Methodology for development of treatment recommendations[1]

Evidence was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology.

Expression of recommendations:

- ***Recommended:*** GRADEd — Strong; based on systematic reviews
- ***Suggested:*** GRADEd — Conditional; based on systematic reviews (intervention benefits likely outweigh harms, despite uncertainty)

Limitations: Two systematic reviews informed the guideline process for XLH management in adults. Limited evidence allowed for only 3 GRADEd recommendations on the use of CRYSVITA in this population. No GRADEd recommendations were made for conventional therapy or lack of treatment due to insufficient high-quality evidence on patient-important outcomes.[2]

Important Safety Information

CONTRAINDICATIONS

CRYSVITA is contraindicated:

- In concomitant use with oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) due to the risk of hyperphosphatemia.
- When serum phosphorus is within or above the normal range for age.
- In patients with severe renal impairment or end stage renal disease because these conditions are associated with abnormal mineral metabolism.

Please see Important Safety Information on back and full Prescribing Information for CRYSVITA in pocket.

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

[a]Guidelines are not sponsored by Kyowa Kirin.

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

Important Safety Information

WARNINGS AND PRECAUTIONS

Hypersensitivity

- Hypersensitivity reactions (e.g., rash, urticaria) have been reported in patients with CRYSVITA. Discontinue CRYSVITA if serious hypersensitivity reactions occur and initiate appropriate medical treatment.

Hyperphosphatemia and Risk of Nephrocalcinosis

- Increases in serum phosphorus to above the upper limit of normal may be associated with an increased 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.

Hypercalcemia

- Increases in serum calcium have been reported in patients treated with CRYSVITA. Patients with risk factors such as pre-existing hyperparathyroidism, prolonged immobilization, dehydration, hypervitaminosis D, or renal impairment, are at higher risk of hypercalcemia. Monitor these patients for serum calcium and parathyroid hormone levels before and during CRYSVITA treatment for moderate to severe hypercalcemia. In patients with moderate to severe hypercalcemia, CRYSVITA should not be administered until hypercalcemia is adequately managed.

Injection Site Reactions

- Administration of CRYSVITA may result in local injection site reactions. Discontinue CRYSVITA if severe injection site reactions occur and administer appropriate medical treatment.

ADVERSE REACTIONS

Pediatric Patients

- Adverse reactions reported in 10% or more of CRYSVITA-treated pediatric XLH patients across three studies are: pyrexia (55%, 44%, and 62%), injection site reaction (52%, 67%, and 23%), cough (52%), vomiting (41%, 48%, and 46%), pain in extremity (38%, 46%, and 23%), headache (34% and 73%), tooth abscess (34%, 15%, and 23%), dental caries (31%), diarrhea (24%), vitamin D decreased (24%, 37%, and 15%), toothache (23% and 15%), constipation (17%), myalgia (17%), rash (14% and 27%), dizziness (15%), and nausea (10%).

Adult Patients

- Adverse reactions reported in more than 5% of CRYSVITA-treated adult XLH patients and in at least 2 patients more than placebo in one study are: back pain (15%), headache (13%), tooth infection (13%), restless legs syndrome (12%), vitamin D decreased (12%), dizziness (10%), constipation (9%), muscle spasms (7%), and blood phosphorus increased (6%).
- 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 Kyowa Kirin, Inc. Adverse Event reporting line at 1-844-768-3544.
- There is no information regarding the presence of CRYSVITA in human milk or the effects of CRYSVITA on milk production or the breastfed infant. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CRYSVITA and any potential adverse effects on the breastfed infant from CRYSVITA or from the underlying maternal condition.

PATIENT COUNSELING INFORMATION

- Advise patients not to use any oral phosphate and/or active vitamin D analog products.
- Instruct patients to contact their physician if hypersensitivity reactions, injection site reactions, and restless legs 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 Kyowa Kirin, Inc. at 1-844-768-3544.

For important risk and use information, please see the full Prescribing Information for CRYSVITA in pocket.

References: 1. Khan AA, Ali DS, Appelman-Dijkstra NM, et al. X-linked hypophosphatemia management in adults: an International Working Group clinical practice guideline. *J Clin Endocrinol Metab.* Published online 2025. doi:10.1210/clinem/dgaf170 **2.** Ali DS, Khan AA, Mirza RD, et al. Methodology for the International Working Group clinical practice guidelines on X-linked hypophosphatemia in children and adults. *J Bone Miner Metab.* 2025;43(3):193-202. doi:10.1007/s00774-025-01585-z

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BUSINESS CARD HOLDER