

**Proposed Addendum to Protocol for Crysvita[®] (burosumab-twza)
April 2026**

Crysvita[®] (burosumab-twza)

Protocol applies to FDA approved biosimilars and related indications and dosages

Addendum:

Reviewed current clinical literature and updated criteria to include additional laboratory parameters used to aid in the diagnosis of both X-linked hypophosphatemia and FGF23-related hypophosphatemia in tumor-induced osteomalacia.

Background:

Crysvita is a fibroblast growth factor 23 (FGF23) blocking antibody indicated for the treatment of X-linked hypophosphatemia (XLH) in patients 6 months and older and for the treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in patients 2 years of age and older.

Criteria for initial approval must meet ALL of the following:

1. The medication requested is prescribed in accordance with a Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with a medically-appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence
2. The patient is of the FDA-labeled or compendial approved age
3. The patient's most recent weight is provided
4. The Medication is prescribed by or in consultation with a geneticist, nephrologist, endocrinologist or a specialist who has appropriate knowledge or experience
5. The patient does not have any contraindications to therapy:
 - a. Concomitant use with oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol)
 - b. Serum phosphorus within or above the normal range for age
 - c. Severe renal impairment or end stage renal disease
6. Prescriber attests oral phosphate and/or active vitamin D analogs have been discontinued one week prior to starting Crysvita
7. Crysvita is administered by a healthcare provider

For X-linked Hypophosphatemia (XLH) (must meet 1 through 4):

1. Patient has evidence of rickets or another bone disease
2. The diagnosis is confirmed by one of the following (documentation is provided):
 - a. Patient's genetic test confirms mutation of the PHEX gene OR
 - b. Genetic test results confirming a PHEX gene mutation in a directly related

- family member (first-degree relative) OR
- c. Serum fibroblast growth factor 23 (FGF23) level above the upper limit of normal or abnormal for laboratory reference range
- 3. Documentation is provided confirming the patient has low serum phosphate levels compared to age-appropriate normal range or laboratory defined normal range
- 4. Patient tried and failed or has an intolerance or contraindication to treatment with oral phosphate and active vitamin D analogs

For Tumor-induced Osteomalacia (TIO) (must meet 1 through 3):

1. The diagnosis is confirmed by ALL of the following (documentation is provided):
 - a. Serum FGF23 level above the upper limit of normal or abnormal for laboratory reference range
 - b. Fasting Serum phosphorus levels below lower limit of normal or abnormal for laboratory reference range
 - c. Tubular maximum reabsorption of phosphate per glomerular filtration rate (TmP/GFR) ratio is below lower limit of normal or abnormal for laboratory reference range, documentation is received ensuring concomitant administration of phosphate supplementation is avoided
2. The tumor cannot be curatively resected or localized (located)
3. Patient tried and failed or has an intolerance or contraindication to treatment with oral phosphate and active vitamin D analogs

Continuation of therapy (must meet 1 through 3):

1. Documentation is provided of serum phosphorus levels, alkaline phosphatase (ALP) levels, or TmP/GFR ratio trending towards or at laboratory normal range
2. Patient has improvement in symptoms (e.g., skeletal pain, linear growth, etc.), improvement in radiographic imaging and/or no evidence of clinical worsening
3. The medication requested is prescribed in accordance with a Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with a medically-appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

Approval Duration and Quantity Restrictions:

Approval: 12 months

Quantity Level Limit:

Crysvita 10mg/mL single dose vial	1 vial per 14 days
Crysvita 20mg/mL single dose vial	9 vials per 14 days
Crysvita 30mg/mL single dose vial	6 vials per 14 days

References:

1. Crysvita (prescribing information). Kyowa Kirin, Inc. Princeton, NJ 08540, August 2025.
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3. Dahir K Roberts MS et al. X-Linked Hypophosphatemia: A New Era in Management. Journal of the Endocrine Society. Volume 4, Issue 12. December 2020. Accessed on September 6, 2022 at:

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5. Haffner D, Francesco E, Seefried L, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphatemia. *Nat Rev Nephrol*. 2025;21(5):330-354.
6. Ali DS, Carpenter TO, Imel EA, et al. X-linked hypophosphatemia management in children: an international working group clinical practice guideline. *J Clin Endocrinol Metab*. 2025;110(7):2055-2070.
7. 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*. 2025;110(8):2353-2370.
8. Dahir K, Zanchetta MB, Stanciu I, et al. Diagnosis and Management of Tumor-induced Osteomalacia: Perspectives from Clinical Experience. *J Endocr Soc*. 2021;5(9):1-12.
9. Álvarez-Rivas N, Lugo-Rodríguez G, Maneiro JR, et al. Tumor-induced osteomalacia: A systematic literature review. *Bone Rep*. 2024;21:1-8.