Draft Revision Policy: Do Not Implement

Burosumab-twza (Crysvita®)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

~~Crysvita is indicated for the treatment of:~~

- Treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.
- Treatment of fibroblast growth factor 23 (FGF23)-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adult and pediatric patients 2 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review ~~for X-linked hypophosphatemia (XLH)~~:

X-linked Hypophosphatemia (XLH)
Initial requests

- ~~Radiographic evidence of rickets or other bone disease attributed to XLH~~
- At least one of the following:
  - Genetic ~~testing~~ test results confirming the member has a ~~PHEX (phosphate regulating gene with homology to endopeptidases located on the X chromosome) mutation~~ pathogenic variant in the phosphate regulating endopeptidases X-linked (PHEX) gene
  - Genetic ~~testing~~ test results confirming a pathogenic variant in the PHEX ~~mutation~~ gene in a directly related family member with appropriate X-linked inheritance
  - Lab test results confirming the member's serum fibroblast growth factor 23 (FGF23) level is above the upper limit of normal or abnormal for the assay.
- Baseline fasting serum phosphate level
- Radiographic evidence of rickets or other bone diseases attributed to XLH

Continuation requests

- Chart notes or medical record documentation showing beneficial response to therapy.

Tumor Induced Osteomalacia (TIO)
Initial requests
- Lab test results confirming the member's serum fibroblast growth factor 23 (FGF23) level is above the upper limit of normal or abnormal for the assay.
- Baseline fasting serum phosphorus ~~levels~~ level
- Ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR)
- Chart notes or medical record documentation of clinical signs or symptoms of TIO

Continuation requests
- Chart notes or medical record documentation showing beneficial response to therapy.

PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an endocrinologist, nephrologist, or a physician specializing in the treatment of metabolic bone disorders.

COVERAGE CRITERIA

X-linked Hypophosphatemia (XLH)

Authorization of 12 months may be granted for treatment of X-linked hypophosphatemia (XLH) when ~~both~~ all of the following criteria are met:
- Member meets one of the following criteria:
  - Genetic ~~testing was conducted to~~ test confirming a pathogenic variant in the PHEX ~~mutation~~ gene in the member.
  - Genetic ~~testing was conducted to~~ test confirming a pathogenic variant in the PHEX ~~mutation~~ gene in a directly related family member with appropriate X-linked inheritance.
  - Member's FGF23 level is above the upper limit of normal or abnormal for the assay.
- Member's baseline fasting serum phosphorus level is below the normal range for age.
- Member has radiographic evidence of rickets or other bone diseases attributed to XLH.

Tumor-induced Osteomalacia (TIO)

Authorization of 12 months may be granted for treatment of tumor-induced osteomalacia (TIO) when ~~both~~ all of the following criteria are met:
- Member's diagnosis is confirmed by ALL of the following:
  - Member's FGF23 level is above the upper limit of normal or abnormal for the assay.
  - Member's baseline fasting serum phosphorus ~~levels are less than 2.5 mg/dL~~ level is below the normal range for age.
  - Member's ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) is ~~less than 2.5 mg/dL~~ below the normal range for age.
- Member has clinical signs or symptoms of TIO (e.g., bone pain, fractures, muscle weakness, limb deformity, craniofacial anomaly, localized mass).
- Member's disease is associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized.

CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section who are currently receiving the requested medication through a paid pharmacy or medical benefit and who are experiencing benefit from therapy as evidenced by disease improvement

or disease stability (e.g., increase or normalization in serum phosphate, improvement in bone and joint pain, reduction in fractures, improvement in skeletal deformities).

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Crysvita (Burosumab-twza)	Tumor-induced Osteomalacia	Route of Administration: Subcutaneous ≥2 year(s) ≥10kg 180mg every 2 weeks
Crysvita (Burosumab-twza)	X-linked hypophosphatemia	Route of Administration: Subcutaneous ≥6 month(s) 90mg every 2 weeks ≥6 month(s) to <18 year(s) <10/kg 2mg every 2 weeks

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Crysvita [package insert]. Princeton, NJ: Kyowa Kirin, Inc.; August 2025.
2. Linglart A, Imel EA, Whyte MP, et al. Sustained Efficacy and Safety of Burosumab, a Monoclonal Antibody to FGF23, in Children With X-Linked Hypophosphatemia. J Clin Endocrinol Metab. 2022;107(3):813-824.
3. Insogna KL, Briot K, Imel EA, et al. A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial Evaluating the Efficacy of Burosumab, an Anti-FGF23 Antibody, in Adults With X-Linked Hypophosphatemia: Week 24 Primary Analysis. J Bone Miner Res. 2018;33(8):1383-1393.
4. ~~Dieter, H.~~ Haffner D, Emma, F, ~~Eastwood, D.M.~~ Seefried L, et.al. Clinical Practice Recommendations for the Diagnosis and Management of X-linked Hypophosphataemia. Nat Rev Nephrol 2025;21(5):330-354.
5. Khan AA, Ali DS, Appelman-Dijkstra et al. X-Linked hypophosphatemia management in adults: An International Working Group clinical practice guideline. J Clin Endocrinol Metab. 2025;110(8):2353-2370.
6. ClinicalTrials.gov. National Library of Medicine (US). Identifier NCT02304367. Study of Burosumab (KRN23) in Adults with Tumor-Induced Osteomalacia (TIO) or Epidermal Nevus Syndrome (ENS). 2020 June 30. Available from: http://clinicaltrials.gov/ct2/show/NCT02304367.
7. ~~Chong WH, Molinolo AA, Chen CC, et.al Tumor-induced Osteomalacia. Endocrine Related Cancer 18:R53-R77 (2011).~~

~~8. Fauconnier C, Roy T, Gillerot G, et al. FGF23: Clinical usefulness and analytical evolution. Clin Biochem. 2019;66:1-12.~~

9. Jan de Beur SM, Minisola S, Xia WB, et al. Global guidance for the recognition, diagnosis, and management of tumor-induced osteomalacia. J Intern Med. 2023;293(3):309-328.

EFFECTIVE DATE

ID_CHS_2025