

## Clinical Policy: Burosumab-twza (Crysvita)

Reference Number: PA.CP.PHAR.11

Effective Date: 10/2018

Last Review Date: 07/2024

### Description

Burosumab-twza (Crysvita<sup>®</sup>) is a fibroblast growth factor 23 (FGF23) blocking antibody.

### FDA Approved Indication(s)

Crysvita is indicated for the treatment of:

- X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older
- 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

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness that Crysvita is **medically necessary** when the following criteria are met:

#### I. Prescriptions That Require Prior Authorization

All prescriptions for Crysvita (burosumab) must be prior authorized.

#### II. Review of Documentation for Medical Necessity

In evaluating a request for prior authorization of a prescription for Crysvita (burosumab), the determination of whether the requested prescription is medically necessary will take into account whether the beneficiary:

1. Is prescribed Crysvita (burosumab) for the treatment of a diagnosis that is indicated in the U.S. Food and Drug Administration (FDA)-approved package labeling OR a medically accepted indication; **AND**
2. Is age-appropriate according to FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature; **AND**
3. Is prescribed a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature; **AND**

4. Is prescribed Crysvisa (burosumab) by or in consultation with an appropriate specialist (e.g., endocrinologist, geneticist, nephrologist, oncologist, rheumatologist, or other specialist experienced in the treatment of patients with metabolic bone disease, etc.); **AND**
5. Does not have a contraindication to Crysvisa (burosumab); **AND**
6. Has a baseline (before treatment) fasting serum phosphate level that is below the reference range for age; **AND**
7. Has laboratory evidence of renal phosphate wasting (i.e., low percent tubular reabsorption of phosphate [%TRP] and/or low fasting tubular maximum reabsorption of phosphate to glomerular filtration rate [TmP/GFR]); **AND**
8. Has a baseline (before treatment) fibroblast growth factor 23 (FGF23) level that is normal or above the assay-specific reference range for age; **AND**
9. For the treatment of X-linked hypophosphatemia (XLH), **both** of the following:
  - a. Has a diagnosis of XLH confirmed by at least **one** of the following:
    - i. Confirmed PHEX gene mutation,
    - ii. Positive family history of XLH,
    - iii. Presence of typical clinical features of XLH (e.g., abnormal gait, lower limb deformity, decreased growth velocity, etc. in children; short stature, osteomalacia, bone pain, osteoarthritis, pseudofractures, stiffness, enthesopathies, poor dental condition, etc. in adults)
  - b. At least **one** of the following:
    - i. Has open epiphyses
    - ii. Is experiencing clinical signs and/or symptoms of XLH (e.g., limited mobility, musculoskeletal pain and/or stiffness, bone fractures or pseudofractures, decreased physical function, renal calculi, etc.);

**AND**

10. For the treatment of tumor-induced osteomalacia (TIO), has a diagnosis of active TIO confirmed by at least **one** of the following:
  - a. Identification and localization of the underlying tumor that is unresectable or pending resection
  - b. Other causes of genetic and acquired renal phosphate-wasting disorders have been reasonably ruled out;

**AND**

11. If a prescription for Crysvida (burosumab) is for a quantity that exceeds the quantity limit, the determination of whether the prescription is medically necessary will also take into account the guidelines set forth in PA.CP.PMN.59 Quantity Limit Override

NOTE: If the beneficiary does not meet the clinical review guidelines listed above but, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the beneficiary, the request for prior authorization will be approved.

**FOR RENEWALS OF PRIOR AUTHORIZATION FOR CRYSVITA**

**(BUROSUMAB):** The determination of medical necessity of a request for renewal of a prior authorization for Crysvida (burosumab) that was previously approved will take into account whether the beneficiary:

1. Experienced an increased fasting serum phosphate level from baseline; **AND**
2. **One** of the following:
  - a. For a beneficiary with open epiphyses, is experiencing clinical benefit from Crysvida (burosumab) based on the prescriber's assessment
  - b. For all other beneficiaries, experienced improvement of the signs and/or symptoms of the condition (e.g., decreased number of fractures, improved fracture healing, improved bone mineralization, decreased fatigue, pain, and/or stiffness, improved functional capacity, etc.);

**AND**

3. Is prescribed a dose to maintain serum phosphorus within the recommended range that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature; **AND**
4. Is prescribed Crysvida (burosumab) by or in consultation with an appropriate specialist (e.g., endocrinologist, geneticist, nephrologist, oncologist, rheumatologist, or other specialist experienced in the treatment of patients with metabolic bone disease, etc.); **AND**
5. Does not have a contraindication to Crysvida (burosumab) (NOTE: Continuation of treatment with Crysvida [burosumab] is not contraindicated when the fasting serum phosphorus level is within the reference range for age); **AND**
6. If a prescription for Crysvida (burosumab) is for a quantity that exceeds the quantity limit, the determination of whether the prescription is medically necessary will also take into account the guidelines set forth in PA.CP.PMN.59 Quantity Limit Override

NOTE: If the beneficiary does not meet the clinical review guidelines listed above but, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the beneficiary, the request for prior authorization will be approved.

**Approval Duration: 6 months**

**III. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration  
FGF23: fibroblast growth factor 23

TIO: tumor-induced osteomalacia  
XLH: X-linked hypophosphatemia

*Appendix B: Therapeutic Alternatives*  
Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): concomitant use with oral phosphates and active vitamin D analogs, initiation of Crysvisa therapy when serum phosphorus is within or above the normal range for age, severe renal impairment or end stage renal disease because these conditions are associated with abnormal mineral metabolism
- Boxed warning(s): none reported

*Appendix D: General Information*

- Laboratory-specific reference ranges for serum phosphorus levels should be used when available; otherwise, the age- and gender-based reference ranges found below may be used:

Females	Males
1-7 years: 4.3-5.4 mg/dL	1-4 years: 4.3-5.4 mg/dL
8-13 years: 4.0-5.2 mg/dL	5-13 years: 3.7-5.4 mg/dL
14-15 years: 3.5-4.9 mg/dL	14-15 years: 3.5-5.3 mg/dL
16-17 years: 3.1-4.7 mg/dL	16-17 years: 3.1-4.7 mg/dL
≥ 18 years: 2.5-4.5 mg/dL	≥ 18 years: 2.5-4.5 mg/dL

- For pediatric patients continuing on Crysvisa therapy, if serum phosphorus is >5 mg/dL, it is recommended to withhold the dose until the serum phosphorus level falls below the reference range per age.
- For adult patients continuing on Crysvisa therapy, if serum phosphorus is above the upper limit of the normal range, it is recommended to withhold the dose until the serum phosphorus level falls below the reference range.

**IV. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
XLH	<p><b><u>Pediatric XLH</u></b></p> <ul style="list-style-type: none"> <li>• Weight &lt; 10 kg: 1 mg/kg rounded to the nearest 1 mg, SC every two weeks</li> </ul>	Pediatric XLH: 2 mg/kg up to 90 mg every two weeks

	<ul style="list-style-type: none"> <li>Weight <math>\geq</math> 10 kg: 0.8 mg/kg rounded to the nearest 10 mg, SC every two weeks</li> </ul> <p>Increase dose up to approximately 2 mg/kg, SC every two weeks to achieve normal serum phosphorus.</p> <p><b><u>Adult XLH</u></b> 1 mg/kg body weight rounded to the nearest 10 mg SC every four weeks.</p> <p>Crysvita should only be administered by a healthcare professional.</p>	Adult XLH: 1 mg/kg up to 90 mg every four weeks
TIO	<p><b><u>Pediatric TIO (2 years and older)</u></b></p> <ul style="list-style-type: none"> <li>Starting dose is 0.4 mg/kg of body weight rounded to the nearest 10 mg SC every two weeks</li> <li>Dose may be increased up to 2 mg/kg</li> </ul> <p><b><u>Adult TIO</u></b></p> <ul style="list-style-type: none"> <li>Starting dose is 0.5 mg/kg SC every four weeks</li> </ul> <p>Dose may be increased up to 2 mg/kg</p>	180 mg, administered every two weeks

**V. Product Availability**

Single-dose vials for injection: 10 mg/mL, 20 mg/mL, 30 mg/mL

**VI. References**

1. Crysvita Prescribing Information. Princeton, NJ: Kyowa Kirin, Inc; March 2023. Available at: [www.crysvita.com](http://www.crysvita.com). Accessed May 10, 2024.
2. Carpenter TO, Imel EA, Holm IA, et al. A clinician’s guide to Xlinked hypophosphatemia. *J Bone Miner Res.* 2011;26(7):1381-1388.
3. Haffner D, Emma F, Eastwood DM, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphatemia. *Nat Rev Nephrol.* 2019;15(7):435-455.
4. Schindeler A, Biggin A, Munns CF. Clinical evidence for the benefits of burosumab therapy for X-linked hypophosphatemia (XLH) and other conditions in adults and children. *Front Endocrinol (Lausanne).* 2020;11:338.
5. Che H, Roux C, Etcheto A, Rothenbuhler A, Kamenicky P, Linglart A, Briot K. Impaired quality of life in adults with X-linked hypophosphatemia and skeletal symptoms. *Eur J Endocrinol.* 2016;174(3):325-333.
6. Athonvarangkul D, Insogna KL. New therapies for hypophosphatemia-related to FGF23 excess. *Calcif Tissue Int.* 2020. doi: 10.1007/s00223-020-00705-3.
7. Scheinman SJ, Carpenter T, Drezner MK. Hereditary hypophosphatemic rickets and tumor-induced osteomalacia. Sterns RH, Geffner ME, Hoppin AG, eds. Waltham, MA: UpToDate Inc. Updated July 8, 2020. Accessed October 1, 2020.

8. Carpenter TO, Miller PD, Weber TJ, et al. Burosumab improved biochemical, skeletal, and clinical features of tumor-induced osteomalacia syndrome. *J Endocr Soc.* 2020;4(Suppl 1):OR29-06. doi: 10.1210/jendso/bvaa046.403.
9. Florenzano P, Hartley IR, Jimenez M, Roszko K, Gafni RI, Collins MT. Tumor-induced osteomalacia. *Calcif Tissue Int.* 2020. doi: 10.1007/s00223-020-00691-6.
10. Chong WH, Molinolo AA, Chen CC, Collins MT. Tumor-induced osteomalacia. *Endocr Relat Cancer.* 2011;18(3):R53-R77.
11. Jan de Beur SM. Tumor-induced osteomalacia. *JAMA.* 2005;294(10):1260-1267.
12. Jan de Beur SM, Minisola S, Xia Wei-bo. Global guidance for the recognition, diagnosis, and management of tumor-induced osteomalacia. *J Intern Med.* 2023;293:309-28.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0584	Injection, burosumab-twza, 1 mg

Reviews, Revisions, and Approvals	Date
Policy created.	10/2018
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/2019
3Q 2020 annual review: clarified weight-based dosing limits in initial and continued approval criteria; removed the requirement for a prior trial of calcitriol plus oral phosphates based on updated clinical trial data demonstrating superiority of Crysvisa over calcitriol plus oral phosphates; updated FDA approved pediatric age extension to $\geq 6$ months from $\geq 1$ year; references reviewed and updated.	07/2020
Aligned policy with Pennsylvania Medical Assistance Program’s prior authorization guidelines	01/2021
3Q 2021 annual review: no significant changes; references reviewed and updated.	07/2021
3Q 2022 annual review: no significant changes; references reviewed and updated.	07/2022
3Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023
3Q 2024 annual review: no significant changes; references reviewed and updated.	07/2024