Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 08/01/2021**
Policy Number: PA.CP.PHAR.11	**Effective Date: 10/2018** **Revision Date: 07/2021**
Policy Name: Burosumab-twza (Crysvita)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

3Q 2021 annual review: no significant changes; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Burosumab-twza (Crysvita)

Reference Number: PA.CP.PHAR.11
Effective Date: 10.17.18
Last Review Date: 07/2021

Coding Implications
Revision Log

Description
Burosumab-twza (Crysvita®) 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 health plans affiliated with 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 Crysvita (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 Crysvita (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 Crysvita (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 Crysvita (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 Crysvita (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 Crysvita (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 Crysvita (burosumab) (NOTE: Continuation of treatment with Crysvita [burosumab] is not contraindicated when the fasting serum phosphorus level is within the reference range for age); **AND**

6. If a prescription for Crysvita (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.

III. Approval Duration: 6 months

IV. 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 Crysvita 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 Crysvita 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 Crysvita 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
XLH	**Pediatric XLH** • Weight < 10 kg: 1 mg/kg rounded to the nearest 1 mg, SC every two weeks	Pediatric XLH: 2 mg/kg up to 90 mg every two weeks

	• Weight ≥ 10 kg: 0.8 mg/kg rounded to the nearest 10 mg, SC every two weeks Increase dose up to approximately 2 mg/kg, SC every two weeks to achieve normal serum phosphorus. **Adult XLH** 1 mg/kg body weight rounded to the nearest 10 mg SC every four weeks. Crysvita should only be administered by a healthcare professional.	Adult XLH: 1 mg/kg up to 90 mg every four weeks
TIO	**Pediatric TIO (2 years and older)** • Starting dose is 0.4 mg/kg of body weight rounded to the nearest 10 mg SC every two weeks • Dose may be increased up to 2 mg/kg **Adult TIO** • Starting dose is 0.5 mg/kg SC every four weeks Dose may be increased up to 2 mg/kg	180 mg, administered every two weeks

VI. Product Availability

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

VII. References

1. Crysvita Prescribing Information. Novato, CA: Ultragenyx Pharmaceutical Inc; June 2020. Available at: www.crysvita.com. Accessed May 10, 2021.
2. Carpenter TO, et al. A clinician's guide to X-linked hypophosphatemia. JBMR 2011; 26(7):1381-8. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/jbmr.340.
3. Haffner D, Emma F, Eastwood DM, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia. Nature Reviews Nephrology 2019 May; 15: 435-455.
4. Athonvarangkul D and Insogna KL. New therapies for hypophosphatemia-related to FGF23 excess. Calcif Tissue Int. 2020. https://doi.org/10.1007/s00223-020-00705-3.
5. Florenzano P, Hartley I, Jimenez M, et al. Tumor-induced osteomalacia. Calcif Tissue Int. 2020. https://doi.org/10.1007/s00223-020-00691-6.

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	P&T Approval Date
Policy created.	10/18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07.17.19	
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 Crysvita over calcitriol plus oral phosphates; updated FDA approved pediatric age extension to ≥ 6 months from ≥ 1 year; references reviewed and updated.	07.20	
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	