Clinical Policy: Burosumab-twza (Crysvita)

Reference Number: LA.PHAR.11
Effective Date: 11.04.23
Last Review Date: 04.04.24 ~~06.14.23~~
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

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 Louisiana Healthcare Connections that Crysvita is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. X-Linked Hypophosphatemia (must meet all)**:**

1. Diagnosis of XLH confirmed by one of the following (a or b):
   a. DNA testing confirms the presence of mutations in the *PHEX* gene;
   b. Elevated serum FGF23 levels;
2. Prescribed by or in consultation with an endocrinologist or metabolic disease specialist;
3. Age ≥ 6 months;
4. Current (within the last 30 days) serum phosphorus levels are one of the following (a or b):
   a. Below the reference range for age and gender (*use laboratory-specific reference ranges if available; otherwise, see Appendix D for ranges*), and member has not received oral phosphate or vitamin D replacement therapy and serum phosphorus;
   b. In normal range, but member remains symptomatic (e.g., rickets, growth impairment, musculoskeletal pain, bone fractures) despite currently receiving oral phosphate and/or vitamin D replacement therapy;
5. Presence of clinical signs and symptoms of the disease (e.g., rickets, growth impairment, musculoskeletal pain, bone fractures);

6. Crysvita is not prescribed concurrently with oral phosphate or vitamin D replacement therapy;
7. Dose does not exceed one of the following (a or b):
   a. Age 6 months to < 18 years: 2 mg/kg up to 90 mg every two weeks;
   b. Age ≥ 18 years: 1 mg/kg up to 90 mg every four weeks.

Approval duration: 6 months

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B. Tumor-Induced Osteomalacia (must meet all)**:**

1. Diagnosis of TIO with confirmed elevated serum FGF23 levels;
2. Prescribed by or in consultation with an endocrinologist or metabolic disease specialist;
3. Age ≥ 2 years;
4. Failure of a ≥ 3 consecutive month trial of oral phosphate and vitamin D replacement therapy, unless contraindicated or clinically significant adverse effects are experienced;
5. Current (within the last 30 days) serum phosphorus levels are one of the following (a or b):
   a. Below the reference range for age and gender (*use laboratory-specific reference ranges if available; otherwise, see Appendix D for ranges*), and member has not received oral phosphate or vitamin D replacement therapy;
   b. In normal range, but member remains symptomatic (e.g., osteomalacia, muscle weakness, fatigue, bone pain, fractures) despite currently receiving oral phosphate and/or vitamin D replacement therapy;
6. Documentation confirms that the causative tumor(s) is/are not amenable to surgical excision or resection;
7. Crysvita is not prescribed concurrently with oral phosphate or vitamin D replacement therapy;
8. Documentation of member's current weight, for dose calculation purposes;
9. Dose does not exceed 2 mg/kg (maximum of 180 mg) every two weeks.

Approval duration: 6 months

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C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. X-Linked Hypophosphatemia (must meet all)**:**

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by both of the following (a and b):

a. An increase in serum phosphorus levels from baseline and/or maintenance within the normal range for age and gender, not to exceed the upper limit of that normal range (*use laboratory-specific reference ranges if available; otherwise, see Appendix D for ranges*);
b. A positive clinical response including any of the following: enhanced height velocity, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain;

3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Age 6 months to < 18 years: 2 mg/kg up to 90 mg every two weeks;
   b. Age ≥ 18 years: 1 mg/kg up to 90 mg every four weeks.

Approval duration: 12 months

B. Tumor-Induced Osteomalacia (must meet all)**:**

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by both of the following (a and b):
   a. An increase in serum phosphorus levels from baseline and/or maintenance within the normal range for age and gender, not to exceed the upper limit of that normal range (*use laboratory-specific reference ranges if available; otherwise, see Appendix D for ranges*);
   b. Documentation confirms improvement in symptoms (e.g., osteomalacia, muscle weakness, fatigue, bone pain, fractures);
3. Documentation of member's current weight, for dose calculation purposes;
4. If request is for a dose increase, new dose does not exceed 2 mg/kg (maximum of 180 mg) every two weeks.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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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 • 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.	Pediatric XLH: 2 mg/kg up to 90 mg every two weeks Adult XLH: 1 mg/kg up to 90 mg every four weeks

Indication	Dosing Regimen	Maximum Dose
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 every two weeks	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~~March 2023. Available at: www.crysvita.com. Accessed May ~~12, 2022~~24, 2023.
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.
6. Dahir K, Zanchetta MB, Stanciu I, et al. Diagnosis and management of tumor-induced osteomalacia: perspectives from clinical experience. J Endocrine Society. September 2021;5(9):bvab099. https://doi.org/10.1210/jendso/bvab099.
7. 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.

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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	LDH Approval Date
Converted corporate to local policy.	06.14.23	10.05.23

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
Annual review: no significant changes; references reviewed and updated.	04.04.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC-level administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.