

Clinical Policy: Burosumab-twza (Crysvita)

Reference Number: ERX.SPA.249

Effective Date: 09.01.18

Last Review Date: 08.21

Line of Business: Commercial, Medicaid

[Revision Log](#)

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

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] 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 \geq 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;
 - 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 \geq 18 years: 1 mg/kg up to 90 mg every four weeks.

Approval duration: 6 months

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 \geq 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. Crysvisa is not prescribed concurrently with oral phosphate or vitamin D replacement therapy;
8. Dose does not exceed 180 mg every two weeks.

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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 a health plan affiliated with Envolve Pharmacy Solutions 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. If request is for a dose increase, new dose does not exceed 180 mg every two weeks.

Approval duration: 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

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 Crysvida 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 Crysvida 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 Crysvida 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	<p><u>Pediatric XLH</u></p> <ul style="list-style-type: none"> • 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 <p>Increase dose up to approximately 2 mg/kg, SC every two weeks to achieve normal serum phosphorus.</p> <p><u>Adult XLH</u></p> <p>1 mg/kg body weight rounded to the nearest 10 mg SC every four weeks.</p> <p>Crysvida should only be administered by a healthcare professional.</p>	<p>Pediatric XLH: 2 mg/kg up to 90 mg every two weeks</p> <p>Adult XLH: 1 mg/kg up to 90 mg every four weeks</p>

Indication	Dosing Regimen	Maximum Dose
TIO	<p><u>Pediatric TIO (2 years and older)</u></p> <ul style="list-style-type: none"> Starting dose is 0.4 mg/kg of body weight rounding to the nearest 10mg SC every two weeks Dose may be increased up to 2 mg/kg <p><u>Adult TIO</u></p> <ul style="list-style-type: none"> 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. Crysvida 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>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.08.18	08.18
3Q 2019 annual review: removed the requirement for a prior trial of calcitriol plus oral phosphates based on updated clinical trial data which demonstrated superiority of Crysvida over calcitriol plus oral phosphates; changed diagnosis confirmation to require only one lab test results based on specialist feedback; added requirement for presence of clinical signs and symptoms; added reauthorization criteria for confirming clinical response to therapy; references reviewed and updated.	05.14.19	08.19
RT4: updated FDA approved pediatric age extension to ≥ 6 months from ≥ 1 year.	10.09.19	
3Q 2020 annual review: clarified weight based dosing limits in initial and continued approval criteria; references reviewed and updated.	04.27.20	08.20
RT2: Criteria added for new FDA indication: TIO; references reviewed and updated.	08.11.20	11.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	05.10.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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