Original Effective Date: 03/01/2016
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Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C14517-A

Crysvita (burosumab-twza)

PRODUCTS AFFECTED

Crysvita (burosumab-twza)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
X-linked hypophosphatemia (XLH), Tumor-induced osteomalacia (TIO)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. X-LINKED HYPOPHOSPHATEMIA (XLH):
   1. Documented Diagnosis of X-linked hypophosphatemia (XLH)
      AND
   2. Documentation diagnosis was confirmed by ONE of the following [DOCUMENTATION REQUIRED]:

a. Member has had a genetic test confirming the diagnosis of X-linked hypophosphatemia via identification of a PHEX mutation
OR
b. Positive family history of XLH
OR
c. Presence of typical clinical features of XLH (e.g., In children: abnormal gait, lower limb deformity, decreased growth velocity, etc. In adults: short stature, osteomalacia, bone pain, osteoarthritis, pseudo fractures, stiffness, enthesopathies, poor dental condition, etc.)

AND

3. Documentation of baseline serum phosphorus level below normal range for age AND baseline tubular reabsorption of phosphorus corrected for glomerular filtration rate (TmP/GFR) below the normal range for age and gender [DOCUMENTATION REQUIRED]
AND
4. Documentation member has failed to respond to phosphate and calcitriol (as indicated by poor healing of existent rickets) despite at least 8 weeks of treatment at maximally tolerated doses
AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Crysvita (burosumab-twza) include: use with oral phosphate and/or active vitamin D analogs, use when serum phosphorus is within or above the normal range for age, and use in patients with severe renal impairment or end stage renal disease.]

B. TUMOR-INDUCED OSTEOMALACIA (TIO):
1. Documented diagnosis of FGF23-related hypophosphatemia produced by an underlying tumor
AND
2. Underlying tumor is not amenable to surgical excision or could not be located
AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Crysvita (burosumab-twza)) include: use with oral phosphate and/or active vitamin D analogs, use when serum phosphorus is within or above the normal range for age, and use in patients with severe renal impairment or end stage renal disease.]

CONTINUATION OF THERAPY:

A. X-LINKED HYPOPHOSPHATEMIA:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation therapy has resulted in clinical improvement from baseline or from the previous authorization, including but not limited to: normalization of serum phosphate or maintenance of normal serum phosphorus levels as evidenced by lab results with reference range; Positive clinical response, or stability of clinical signs and symptoms (including but not limited to): enhanced height velocity, enhanced mobility, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain, or clinically significant improvement from baseline in bone health

B. TUMOR-INDUCED OSTEOMALACIA (TIO):
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill

history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND

2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation therapy has resulted in clinical improvement from baseline or from the previous authorization, including but not limited to improvement of serum phosphate or maintenance of normal serum phosphorus levels as evidenced by lab results with reference range; improvement in bone pain, muscle weakness, difficulty walking, muscle spasms, cramps, or tingling/numbness

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with an endocrinologist, nephrologist, rheumatologist, orthopedic specialist, or physician experienced in the treatment of metabolic bone disorders. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
X-LINKED HYPOPHOSPHATEMIA: 6 months of age and older
TUMOR-INDUCED OSTEOMALACIA: 2 years of age and older

QUANTITY:
X-LINKED HYPOPHOSPHATEMIA (XLH):
Pediatric <10 kg: Starting dose is 1 mg/kg every 2 weeks, rounded to nearest 1 mg
Pediatric ≥ 10 kg: Starting dose 0.8 mg/kg every 2 weeks, rounded to nearest 10 mg
Dose may be increased to 2 mg/kg (max dose 90 mg) every 2 weeks.
Adult: 1 mg/kg every 4 weeks, rounded to nearest 10 mg, maximum 90 mg
Quantity limited to smallest vial size available to minimize waste.

TUMOR-INDUCED OSTEOMALACIA (TIO):
Pediatric: Starting dose is 0.4 mg/kg every 2 weeks, rounded to the nearest 10 mg
Adult: Starting dose is 0.5 mg/kg every four weeks
Dose may be increased up to 2 mg/kg not to exceed 180 mg, administered every two weeks.
Quantity limited to smallest vial size available to minimize waste.

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Crysvita (burosumab-twza). For information on site of care, see: Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous injection by a healthcare provider

DRUG CLASS:
X-Linked Hypophosphatemia (XLH) Treatment - Agents

FDA-APPROVED USES:

Indicated for:

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

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

APPENDIX:

Fasting serum phosphorus reference ranges for age (or as indicated by lab):

1 to 3 years: 3.8 to 6.5 mg/dL
4 to 11 years: 3.7 to 5.6 mg/dL
12 to 15 years: 2.9 to 5.4 mg/dL
16 to 19 years: 2.7 to 4.7 mg/dL

Age-Based Normal TmP/GFR Reference[4] Intervals

Age	Sex	Range (mg/dL)	Range (mmol/L)
Birth	Both	3.6 - 8.6	1.43 - 3.43
3 mos	Both	3.7 - 8.25	1.48 - 3.30
6 mos	Both	2.9 - 6.5	1.15 - 2.60
2-15 yrs	Both	2.9 - 6.5	1.15 - 2.44
25-35 yrs	Male	2.5 - 3.4	1.00 - 1.35
25-35 yrs	Female	2.4 - 3.6	0.96 - 1.44
45-55 yrs	Male	2.2 - 3.4	0.90 - 1.35
45-55 yrs	Female	2.2 - 3.6	0.88 - 1.42
65-75 yrs	Both	2.0 - 3.4	0.80 - 1.35

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

X- linked hypophosphatemia (XLH) also called hereditary hypophosphatemic rickets; X-linked dominant hypophosphatemic rickets, X- linked vitamin D-resistant rickets). A rare, hereditary, progressive disorder caused by a mutation in the phosphate regulating endopeptidase (PHEX) gene. Characterized by renal phosphate wasting due to an overproduction of fibroblast growth factor 23 (FGF23), a hormone that promotes urinary phosphate* excretion and suppresses renal production of active Vitamin D (1, 25 dihydroxy vitamin D) *Phosphate plays a critical role in the formation and growth of bones in childhood and helps maintain bone strength in adults; phosphate levels are controlled in large part by the kidneys. The kidneys normally rid the body of excess phosphate by excreting it in urine, and reabsorb phosphorus into the bloodstream when more is needed Crysvita (burosumab-twza) binds to and inhibits the biological activity of FGF23 restoring renal phosphate reabsorption and increasing the serum concentration of 1, 25 dihydroxy vitamin D. In pediatric patients, XLH results in rickets/osteomalacia that leads to lower- extremity deformities, slowed growth, dental abnormalities, and reduced height. Adults with XLH experience osteomalacia and often have severe joint, bone and tooth pain and an increased incidence of stress fractures/pseudo-fractures, particularly in the lower extremities. The most prevalent genetic form of rickets or osteomalacia; XLH affects an estimated 3,000 children and 12,000adults in the United States (FDA 2018) Current care options for XLH include supplements of multiple daily doses of phosphate and high-dose calcitriol (the active form of Vitamin D), growth hormones, corrective surgery,

and dental treatment. The long-term outlook for patients with XLH varies depending on severity and whether complications arise.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Crysvita (burosumab-twza) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Crysvita (burosumab-twza) include: use with oral phosphate and/or active vitamin D analogs, use when serum phosphorus is within or above the normal range for age, and use in patients with severe renal impairment or end stage renal disease.

OTHER SPECIAL CONSIDERATIONS:

If a patient misses a dose, resume Crysvita as soon as possible at the prescribed dose. To avoid missed doses, treatments may be administered 3 days either side of the scheduled treatment date.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
J0584	Injection, burosumab-twza 1mg

AVAILABLE DOSAGE FORMS:

Crysvita SOLN 10 MG/ML single-dose vial
Crysvita SOLN 20 MG/ML single-dose vial
Crysvita SOLN 30 MG/ML single-dose vial

REFERENCES

1. Crysvita (burosumab-twza) injection, for subcutaneous use [prescribing information]. Novato, CA: Ultragenyx Pharmaceutical; March 2023.
2. Carpenter TO, Whyte MP, Imel EA, et al. Burosumab Therapy in Children with X-Linked Hypophosphatemia. N Engl J Med. 2018 May 24;378(21):1987-1998. doi: 10.1056/NEJMoa1714641.
3. Munns CF, Shaw N, Kiely M, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. The Journal of Clinical Endocrinology and Metabolism. 2016;101(2):394-415. doi:10.1210/jc.2015-2175.
4. Ruppe MD. X-Linked Hypophosphatemia. 2012 Feb 9 [Updated 2017 Apr 13]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. Table 2. [Age-Based Normal TmP/GFR Reference Intervals]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK83985/

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Continuation of Therapy Quantity References	Q3 2025
REVISION- Notable revisions: Required Medical Information Other Special Considerations	Q3 2024
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Prescriber Requirements Quantity FDA-Approved Uses Contraindications/Exclusions/Discontinuation References	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file