Crysvita® (burosumab-twza)
(Subcutaneous)

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 12 months thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- **XLH:** 90 billable units every 14 days
- **TIO:** 180 billable units every 14 days

III. Initial Approval Criteria [1-12]

Site of care specialty infusion program requirements are met (refer to Moda Site of Care Policy).

Coverage is provided in the following conditions:

- Patient has not received oral phosphate and/or active vitamin D analogs within 1 week prior to the start of therapy; **AND**
- Baseline fasting serum phosphorus* level with current hypophosphatemia, defined as a phosphate level below the lower limit of the laboratory normal reference range; **AND**
- Patient has a reduced tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR); **AND**
- Other causes of hypophosphatemia (e.g., autosomal dominant or recessive hypophosphatemic rickets) have been ruled out; **AND**

***Note:** Phosphorous levels should be obtained fasting 12 hours or more without food or drink except for water and after an adequate washout period after supplements; lab values (i.e. GFR, phosphorous, TmP/GFR) should be obtained within 28 days of the date of administration.*

Universal Criteria

- Must be prescribed by, or in consultation with, a nephrologist or endocrinologist; **AND**

- Will not be used concomitantly with oral phosphate and/or active vitamin D analogs; **AND**
- Patient does not have severe renal impairment, defined as a glomerular filtration rate (GFR) of <30 mL/min; **AND**
- Patient 25-hydroxy vitamin D levels will be monitored at baseline and intermittently and patient will be supplemented with cholecalciferol or ergocalciferol to maintain levels in the normal range for age; **AND**

X-linked Hypophosphatemia (XLH) † Φ

- Patient is at least 6 months of age; **AND**
- Diagnosis is confirmed by identifying at least one of the following:
  - Serum fibroblast growth factor-23 (FGF23) level > 30 pg/mL (>230 RU/mL in children 3 months-17 years; >180 RU/mL in adults using EDTA plasma); **OR**
  - Phosphate regulating gene with homology to endopeptidases located on the X chromosome (*PHEX*gene) mutations in the patient; **AND**
- Adult patients must have had an inadequate response from oral phosphate and active vitamin D analogs

Tumor-induced Osteomalacia (TIO) † Φ

- Patient is at least 2 years of age; **AND**
- Must have a diagnosis of tumor-induced osteomalacia associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized; **AND**
- Diagnosis is confirmed by identifying excessive serum FGF23 (i.e., level ≥ 100 pg/mL) that is not amenable to cure by surgical excision of the offending tumor/lesion

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1-3,9,10,12]

Coverage may be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria as identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe hypersensitivity reactions, hyperphosphatemia and/or nephrocalcinosis, severe injection site reactions, etc.; **AND**
- Current serum phosphorus level is not above the upper limit of the laboratory normal reference range; **AND**

- Disease response as indicated by increased serum phosphorus levels, improvement in renal phosphate wasting, a reduction in serum total alkaline phosphatase activity, improvement in symptoms (e.g., skeletal pain, linear growth, etc.), and/or improvement in radiographic imaging of Rickets/osteomalacia; **AND**

X-linked Hypophosphatemia (XLH) [9,12]

- Pediatric patients must be re-evaluated at adulthood in order to determine if continued therapy is necessary (i.e., discontinuation of burosumab in order to reassess whether treatment with oral phosphate and active vitamin D analogs provide an adequate response)

Tumor-induced Osteomalacia (TIO) [10,12]

- If a patient undergoes treatment of the underlying tumor (i.e., surgical excision or radiation therapy) treatment should be interrupted and serum phosphorus reassessed after treatment has been completed to determine if continued therapy is necessary

V. Dosage/Administration [1]

Indication	Dose**
X-Linked Hypo-phosphatemia (XLH)	*Pediatrics* Weight <10 kg: • Starting dose is 1 mg/kg of body weight, rounded to the nearest 1 mg, administered every two weeks. Weight ≥10 kg: • Starting dose is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, administered every two weeks. • The minimum starting dose is 10 mg up to a maximum dose of 90 mg. – *Measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment, and thereafter as appropriate.* – *If serum phosphorus is below the reference range for age, dose may be increased (please refer to prescribing information for stepwise dose increase schedule).* – *If serum phosphorous is above 5 mg/dL, withhold treatment. Once serum phosphorus is below the reference range for age, treatment may be restarted (please refer to prescribing information for re-initiation dose schedule).*
	Adults • Starting dose is 1 mg/kg body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, administered every four weeks. – *Assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate.*

	– *If serum phosphorus is above the normal range, withhold the next dose. Once serum phosphorus is below the normal range, treatment may be restarted (please refer to prescribing information for re-initiation dose schedule).*
Tumor-induced Osteomalacia (TIO)	*Pediatrics* • Starting dose is 0.4 mg/kg of body weight, rounded to the nearest 10 mg, administered every two weeks, up to a maximum dose of 2 mg/kg not to exceed 180 mg administered every two weeks. – *After initiation of treatment, assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate.* – *If serum phosphorus is within the reference range for age, continue with the same dose.* – *Reassess fasting serum phosphorus level 4 weeks after dose adjustment (please refer to prescribing information for stepwise dose increase and decrease schedule).* – *If a patient undergoes treatment of the underlying tumor (i.e., surgical excision or radiation therapy), treatment should be interrupted and serum phosphorus reassessed after treatment has been completed. Dose should be restarted at the patient's initiation dose if serum phosphorus remains below the lower limit of normal (please refer to prescribing information for dose adjustment schedule).*
	Adults • Starting dose is 0.5 mg/kg body weight, rounded to the nearest 10 mg up to a maximum dose of 180 mg, administered every 2 weeks. – *After initiation of treatment with, assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate.* – *If serum phosphorus is within the normal range, continue with the same dose.* – *If serum phosphorus is below the normal range, the dose should be titrated (please refer to prescribing information for stepwise dose -adjustment schedule).* – *If a patient undergoes treatment of the underlying tumor (i.e., surgical excision or radiation therapy), treatment should be interrupted and serum phosphorus reassessed after treatment has been completed. Dose should be restarted at the patient's initiation dose if serum phosphorus remains below the lower limit of normal (please refer to prescribing information for dose adjustment schedule).*
***Note**: Do not adjust the Crysvita dose more frequently than every 4 weeks, refer to the package insert for dose adjustments. Crysvita must be administered via subcutaneous injection by a healthcare provider.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J0584 – Injection, burosumab-twza 1 mg; 1 billable unit = 1 mg

NDC(s):

- Crysvita 10 mg/mL single-dose vial: 42747-0102-xx
- Crysvita 20 mg/mL single-dose vial: 42747-0203-xx
- Crysvita 30 mg/mL single-dose vial: 42747-0304-xx

VII. References

1. Crysvita [package insert]. Princeton, NJ; Kyowa Kirin, Inc.; March 2023. Accessed May 2025.
2. Whyte MP, Portale A, Imel E, Boot A, Hogler W, et al. Burosumab (KRN23), a fully human anti-FGF23 monoclonal antibody for X-linked hypophosphatemia (XLH): final 64-week results of a randomized, open-label, phase 2 study of 52 children (meeting abstract). J Bone Miner Res. 2017;32(S1)
3. Imel E, Carpenter T, Gottesman GC, et al. The effect of burosumab (KRN23), a fully human anti-FGF23 monoclonal antibody, on phosphate metabolism and rickets in 1 to 4-year-old children with X-linked hypophosphatemia (XLH). (Meeting abstract). J Bone Miner Res. 2017;32(S1)
4. Laurent MR, Harvengt P, Mortier GR, et al. X-Linked Hypophosphatemia. 2012 Feb 9 [Updated 2023 Dec 14]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK83985/
5. Linglart A, Biosse-Duplan M, Briot K, et al. Therapeutic management of hypophosphatemic rickets from infancy to adulthood. Endocr Connect. 2014 Mar 1; 3(1): R13–R30.
6. Carpenter TO, Imel EA, Holm IA, et al. A clinician's guide to x-linked hypophosphatemia. J Bone Miner Res. 2011 Jul; 26(7): 1381–1388.
7. Felsenfeld AJ, Levine BS. Approach to treatment of hypophosphatemia. Am J Kidney Dis. 2012 Oct;60(4):655-61.
8. Chong W, Molinolo A, Chen C, et al. Tumor-induced osteomalacia. Endocr Relat Cancer. 2011 Jun; 18(3): R53–R77. Published online 2011 Jun 8. doi: 10.1530/ERC-11-0006
9. Haffner D, Emma F, Seefried L, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia [published correction appears in Nat Rev Nephrol. 2025 May;21(5):355. doi: 10.1038/s41581-025-00939-0.]. *Nat Rev Nephrol*. 2025;21(5):330-354. doi:10.1038/s41581-024-00926-x
10. Hartley IR, Roszko KL. Treatment Advances in Tumor-Induced Osteomalacia. Calcif Tissue Int. 2025 Jan 4;116(1):24. doi: 10.1007/s00223-024-01317-x. PMID: 39755803; PMCID: PMC11700048.

11. Hartley IR, Gafni RI, Roszko KL, et al. Determination of FGF23 Levels for the Diagnosis of FGF23-Mediated Hypophosphatemia. *J Bone Miner Res*. 2022;37(11):2174-2185. doi:10.1002/jbmr.4702
12. Scheinman SJ, Carpenter T. (2024). Hereditary hypophosphatemic rickets and tumor-induced osteomalacia. In Sterns RH, Geffner ME. (Eds.), *UptoDate.* Last updated Dec 18, 2024. Accessed June 17, 2025. Available from https://www.uptodate.com/contents/hereditary-hypophosphatemic-rickets-and-tumor-induced-osteomalacia.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E83.31	Familial hypophosphatemia
E83.39	Other disorders of phosphorus metabolism
M83.8	Other adult osteomalacia

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC