MEDICAL MUTUAL®

Drug Policy

Policy:	**201812-MRx** **(v05-22)**	**Initial Effective Date: 06/17/2018** **Annual Review Date: 05/18/2023** **Last Revised Date: 05/18/2023**
Code(s):	**HCPCS J0584**	
SUBJECT:	**Crysvita® (burosumab-twza injection for subcutaneous use – Ultragenyx)**	

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

POLICY STATEMENT

This policy involves the use of Crysvita. Prior authorization is recommended for medical benefit coverage of Crysvita. Approval is recommended for those who meet the conditions of coverage in the **Initial Approval and Renewal Criteria, Preferred Drug (when applicable), Dosing/Administration, Length of Authorization, and Site of Care (when applicable)** for the diagnosis provided. The requirement that the patient meet the Criteria and Preferred Drug for coverage of the requested medication applies to the initial authorization only. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Crysvita is recommended in those who meet the following criteria:

Coverage is provided in the following conditions:

- Patient has not received oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) 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 *(Note: serum phosphorus levels should be monitored periodically throughout therapy, required on renewal)*; **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**

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 (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol); **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 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

**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.*

I. Renewal Criteria[1,2,3]

Authorizations can be renewed based on the following criteria:

- Patient continues to meet 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, 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**
- Pediatric patients must be re-evaluated at adulthood or upon closure of bony epiphyses (whichever occurs first) 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); **AND**
- *(Tumor-Induced Osteomalacia only):* 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.

II. 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).*
	<u>*Adults**</u> • 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	<u>*Pediatrics**</u> •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)*
	<u>*Adults**</u> • 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.*	

III. Billing Code/Availability Information

HCPCS code:

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

NDC:

- Crysvita 10 mg/mL single-dose vial: 69794-0102-xx
- Crysvita 20 mg/mL single-dose vial: 69794-0203-xx
- Crysvita 30 mg/mL single-dose vial: 69794-0304-xx

IV. References

1. Crysvita [package insert]. Novato, CA; Ultragenyx, Pharm.; June 2020. Accessed March 2022.
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. 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; 1993-2018. 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

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

FOR MEDICAL BENEFIT REQUESTS:

Prior approval is required for HCPCS Codes J0584