Crysvita® (burosumab-twza)
(Subcutaneous)

Document Number: IC-0362

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I. Length of Authorization

Initial coverage will be provided for 6 months and may be renewed every 12 months thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Crysvita 10 mg/mL vial: 1 vial every 14 days
- Crysvita 20 mg/mL vial: 1 vial every 14 days
- Crysvita 30 mg/mL vial: 3 vials every 14 days

B. Max Units (per dose and over time) [Medical Benefit]:

- 90 billable units every 14 days (pediatrics)
- 90 billable units every 28 days (adults)

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 1 year of age; **AND**
- Patient has not received oral phosphate and/or active vitamin D analogs within 1 week prior to the start of therapy; **AND**
- Must be prescribed by, or in consultation with, a nephrologist or endocrinologist; **AND**

X-linked Hypophosphatemia (XLH) †

- 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**
- Patient has a reduced tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR); **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 does not have severe renal impairment, defined as a glomerular filtration rate (GFR) of <30 mL/min; **AND**
- Adult patients must have had an inadequate response from oral phosphate and active vitamin D analogs

† FDA Approved Indication(s)

**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.*

IV. Renewal Criteria

Authorizations can be renewed based on the following criteria:

- Patient continues to meet the criteria 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)

V. Dosage/Administration

Indication	Dose
X-Linked Hypophosphatemia (XLH)	*Pediatrics** • 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 above the lower limit of the reference range for age and below 5 mg/dL, continue treatment with the same dose.*
	*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 within the normal range, continue with the same dose.
***Note**: Do not adjust the Crysvita dose more frequently than every 4 weeks. Crysvita must be administered via subcutaneous injection by a healthcare provider*	

VI. Billing Code/Availability Information

HCPCS:

- 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

VII. References

1. Crysvita [package insert]. Novato, CA; Ultragenyx, Pharm.; September 2018. Accessed April 2019.
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.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E83.30	Disorder of phosphorus metabolism, unspecified
E83.31	Familial hypophosphatemia

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

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 Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered 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.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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