Crysvita® (burosumab-twza)
(Subcutaneous)

Document Number: IC-0362

Last Review Date: 05/02/2022
Date of Origin: 05/01/2018
Dates Reviewed: 05/2018, 05/2019, 11/2019, 05/2020, 07/2020, 05/2021, 05/2022

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) [NDC unit]:

- 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: 6 vials every 14 days

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

- **XLH**
  - 90 billable units every 14 days (pediatrics)
  - 90 billable units every 28 days (adults)
- **TIO**
  - 180 billable units every 14 days

III. Initial Approval Criteria[1,2,3,4,5,6,7,8]

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.*

IV. 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.

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).*
	*Pediatrics**

Tumor-induced Osteomalacia	• 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:

- 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.; 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

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E83.30	Disorder of phosphorus metabolism, unspecified
E83.31	Familial hypophosphatemia
E83.39	Other disorders of phosphorus metabolism

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), Local Coverage Articles (LCAs) 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.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 GBA, 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

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- Qualified sign language interpreters
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Provides free language services to people whose primary language is not English, such as:

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If you believe that PCHP has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Grievance Specialist
PreferredOne Community Health Plan
PO Box 59052
Minneapolis, MN 55459-0052
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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PreferredOne Insurance Company
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Minneapolis, MN 55459-0212
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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