

Crysvita® (burosumab-twza) (Subcutaneous)

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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 \geq 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/Administration¹

Indication	Dose
X-Linked Hypo-phosphatemia (XLH)	<u><i>Pediatrics*</i></u>
	Weight <10 kg: <ul style="list-style-type: none"> • Starting dose is 1 mg/kg of body weight, rounded to the nearest 1 mg, administered every two weeks. Weight ≥10 kg: <ul style="list-style-type: none"> • 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. <ul style="list-style-type: none"> – <i>Measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment, and thereafter as appropriate.</i> – <i>If serum phosphorus is below the reference range for age, dose may be increased (please refer to prescribing information for stepwise dose increase schedule).</i> – <i>If serum phosphorus 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).</i>
	<u><i>Adults*</i></u> <ul style="list-style-type: none"> • 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. <ul style="list-style-type: none"> – <i>Assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate.</i> – <i>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).</i>
	<u><i>Pediatrics*</i></u>

Tumor-induced Osteomalacia	<ul style="list-style-type: none"> • 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. – <i>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</i> – <i>If serum phosphorus is within the reference range for age, continue with the same dose</i> – <i>Reassess fasting serum phosphorus level 4 weeks after dose adjustment (please refer to prescribing information for stepwise dose increase and decrease schedule)</i> – <i>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)</i>
	<p><u>Adults*</u></p> <ul style="list-style-type: none"> • 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. – <i>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</i> – <i>If serum phosphorus is within the normal range, continue with the same dose.</i> – <i>If serum phosphorus is below the normal range, the dose should be titrated (please refer to prescribing information for stepwise dose adjustment schedule)</i> – <i>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)</i>
<p>*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.</p>	

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. Crysvida [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

Nondiscrimination & Language Access Policy

Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, sex, sexual orientation, or gender identity. We do not exclude people or treat them differently because of race, color, national origin, age, disability, sex, sexual orientation, or gender identity.

We will:

Provide free aids and services to people with disabilities to communicate effectively with us, such as:

- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provide free language services to people whose primary language is not English, such as:

- Qualified interpreters
- Information written in other languages

If you need these services, contact us at the phone number shown on the inside cover of this contract, your id card, or aspirushealthplan.com.

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

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1062
Minneapolis, MN 55440
Phone: 1.866.631.5404 (TTY: 711)
Fax: 763.847.4010
Email: customerservice@aspirushealthplan.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Nondiscrimination Grievance Coordinator 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>.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë. Telefononi në 1.866.631.5404 (TTY: 711).

Arabic: تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلی رقم الهاتف 1.866.631.5404 (رقم هاتف الصم والبك : 711)

French: ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelezle 1.866.631.5404 (ATS : 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1.866.631.5404 (TTY: 711).

Hindi: _यान द_ : य_द आप िहंदी बोलते ह_ तो आपके िलए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_। 1.866.631.5404 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.866.631.5404 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1.866.631.5404 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 1.866.631.5404 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1.866.631.5404 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.866.631.5404 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1.866.631.5404 (TTY: 711)

Traditional Chinese: 注意: 如果您使用繁體中文, 您可以免費獲得語言援助服務。請致電 1.866.631.5404 (TTY: 711)。

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1.866.631.5404 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1.866.631.5404 (TTY: 711).

Lao: ໄປດຊາຍ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັຽຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທ 1.866.631.5404 (TTY: 711).