Department:	Pharmacy Management	**Original Approval:**	10/12/2020
Policy No:	PM163	**Last Approval:**	11/14/2025
Policy Title:	Burosumab (Crysvita) injection Clinical Coverage Criteria		
Approved By:	UM Criteria Subcommittee		
Applicable Line(s) of Business:	☐ **Washington Apple Health (Medicaid)** ☐ **Behavioral Health Services Only** ☐ **Apple Health Expansion** ☒ **Medicare Advantage/Special Needs Plan** ☒ **Medicare Advantage Only** ☒ **Cascade Select**		

Required Clinical Documentation for Review

Documentation required to determine medical necessity for Burosumab (Crysvita):

- History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service
- Diagnosis
- Labs/Diagnostics
- Dosing and duration requested
- Initial/Extended approval
- Medical records from the last 6 months showing the patient's problems, history, prior treatments, response to treatment, imaging and laboratory studies, details of the skilled needs, details of any specific needs related to risk/trauma/cultural etc., assessment and plan
- Prescribed by or in consultation with a specialist, when indicated

Background

Burosumab (Crysvita), a fibroblast growth factor 23 (FGF23) blocking antibody, is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients ≥ 6 months of age and for the treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adult and pediatric patients 2 years of age and older.[1] Burosumab (Crysvita) is a recombinant human immunoglobulin G subclass 1 (IgG1) anti-FGF antibody. FGF23 reduces renal tubular phosphate reabsorption and suppresses renal production of 1,24 dihydroxyvitamin D. Via inhibition of FGF23 activity, Burosumab (Crysvita) restores renal phosphate reabsorption and increases serum concentrations of 1,25 dihydroxyvitamin D. Burosumab (Crysvita) is administered as a subcutaneous (SC) injection by a

healthcare provider. It is given once every 2 weeks (Q2W) in pediatric patients 6 months to < 18 years of age and once every 4 weeks (Q4W) in patients ≥ 18 years of age for the treatment of XLH. It is given once Q4W in both pediatric and adult patients for the treatment of TIO.

Disease Overview

XLH is a dominant inherited disease of renal phosphate wasting.[2-4] While it is rare, it is the most common form of hereditary rickets and is estimated to occur in one out of every 20,000 live births. The pathogenesis of XLH is not fully understood; however, an inactivating genetic mutation in phosphate regulating endopeptidase on the X chromosome (PHEX) leads to elevated FGF23. Increased levels of FGF23 increased renal excretion of phosphate and abnormal regulation of vitamin D metabolism. Patients with XLH experience hypophosphatemic rickets (or osteomalacia [i.e., accumulation of unmineralized osteoid/softening of the bones]).[2,3,5] The majority of patients present in the first 2 years of life with bowing deformities of the lower extremities and short stature. In adults, the primary symptom in adults is enthesopathy (i.e., calcification of tendons, ligaments, and joint capsules), which is associated with joint pain and impaired mobility. These patients may also experience spontaneous dental abscesses, stress fractures, and sensorineural hearing loss. The XLH diagnosis can be established in patients with a low serum phosphate concentration, a reduced tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR), an inappropriate calcitriol level for the severity of hypophosphatemia, and/or by identification on molecular genetic testing of a hemizygous PHEX pathogenic variant in a male patient or a heterozygous PHEX pathogenic variant in a female patient. Genetic testing is estimated to identify mutations in the PHEX gene in approximately 70% of patients with hypophosphatemic rickets and 85% to 90% of patients who have familial hypophosphatemic rickets.[6]

TIO is an ultrarare disease caused by tumors secreting FGF23.[7] Most patients have phosphaturic mesenchymal tumors, which are often small and occur in soft tissue or bone, making localization difficulty and delaying diagnosis. Clinical manifestations include osteomalacia, fractures, musculoskeletal pain, fatigue sever myopathy, and reduced health-related quality of life. Biochemical hallmarks of TIO are low serum phosphate levels, phosphaturia, and low or inappropriately normal levels of serum calcitriol.[3]

Prior to the approval of Burosumab (Crysvita), medical therapy for adults and children with XLH consisted of oral phosphate and activated vitamin D (calcitriol).[2,3] This therapy is cumbersome and can result in adverse events (AEs) such as hypercalcemia, hyperparathyroidism, hypercalciuria, nephrolithiasis, nephrocalcinosis, and possibly chronic kidney disease. This therapy often leads to suboptimal response and skeletal abnormalities persist. Definitive treatment for TIO is complete tumor resection. If tumor resection is not possible,

supplementation of oral phosphate and active vitamin D analogues is required. However, efficacy of supplementation therapy is limited.[7]

Clinical Efficacy

The efficacy of Burosumab (Crysvita) was established in three pivotal trials, including two open-label, 64-week studies in pediatric patients and one double-blind, 24-week study in adult patients with XLH.[1] In pivotal studies, patients had baseline serum phosphorus levels less than the lower limit of normal for age.[1,8-10] Across the studies, Burosumab (Crysvita) was found to increase mean serum phosphorus levels significantly from baseline. Radiographic improvements and healing of fractures/pseudofractures were also observed. In a single-arm extension of the adult study, normalization of serum phosphorous was maintained during an additional 24 weeks of Burosumab (Crysvita) therapy.[11] Additional improvements in healing of fractures/pseudofractures were also observed.

One randomized, active-controlled, open-label, phase III study (published) [n = 61] compared Burosumab (Crysvita) and conventional therapy in patients 1 to 12 years of age with XLH.[11] Following 64 weeks of therapy, patients receiving Burosumab (Crysvita) had demonstrated a significantly greater improvement in the Radiographic Global Impression of Change global score compared with the conventional therapy group. Overall, rickets severity, growth, and biochemistries were significantly improved with Burosumab (Crysvita) vs. conventional therapy.

A single group, open label, phase II study (published) [n = 14] evaluated Burosumab (Crysvita) in adult patients with a confirmed diagnosis of FGF23-related hypophosphatemia produced by an underlying tumor that was not amendable to surgical excision or could not be located.[7] Most measure of osteomalacia were improved at week 48: osteoid volume/bone, osteoid thickness, and mineralization lag time decreased. Patients reported a reduction in pain and fatigue and an increase in physical health. Overall, data showed that Burosumab (Crysvita) restored phosphate homeostasis and improved osteomalacia, fracture healing, and functional mobility.

Safety and effectiveness for Burosumab (Crysvita) in pediatric patients 2 years and older with TIO are supported by evidence from the studies in adult patients with TIO with additional modeling and simulation of pharmacokinetic data from adult and pediatric XLH patients and adult TIO patients to inform dosing.[1]

Guidelines

In 2025, an expert panel published Clinical Practice Recommendations for the Diagnosis and Management of XLH.[16] This document recommends that clinicians consider Burosumab (Crysvita) therapy in pediatric patients ≥ 1 year of age and adolescents with signs of rickets (e.g.

leg deformities, elevated total alkaline phosphatase, radiologic evidence) at time of XLH diagnosis. It is also recommended that pediatric patients ≥ 1 year of age and adolescents who are taking oral phosphate and active vitamin D be switched to Burosumab (Crysvita) therapy if there is insufficient skeletal response, significant adverse effects, inability to adhere to oral therapy, or persistent short stature. In adults who have active, symptomatic XLH, guidelines recommend first-line therapy with oral phosphorus and active vitamin D. It is also recommended that adults who are taking oral phosphate and active vitamin D be switched to Burosumab (Crysvita) therapy if there is evidence of pseudofractures, insufficient musculoskeletal response to oral therapy, or intolerance to oral therapy.

In 2021, an expert panel published Reports and Recommendations for the Diagnosis and Management of Tumor-Induced Osteomalacia.[13] This document recommends that surgical resection of the tumor remain the first line of therapy for patients with TIO. In patients in whom the tumor cannot be identified or completely resected, oral phosphate and vitamin D analogues or Burosumab (Crysvita) are recommended treatment options.

Definitions

None.

Indications/Criteria

AH-IMC members	***Excluded benefit. Authorization and billing required directly through WA Apple Health Fee for Service only. Call 800-562-3022.***
Cascade Select members	***Continue to criteria for approval below.***
Medicare Members	***Continue to criteria for approval below.***

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

FDA-Approved Indications

1. **X-Linked Hypophosphatemia (XLH).** Approve Burosumab (Crysvita) for 6 months if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following criteria (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is 6 months of age or older; AND

ii. Diagnosis of X-linked hypophosphatemia is confirmed by ONE of the following (1, 2, or 3):
- **(1)** Genetic testing results confirming PHEX-gene mutation; OR
- **(2)** Genetic testing results confirming a PHEX-gene mutation in a directly related family member with a low serum phosphate and increased alkaline phosphatase activity; OR
- **(3)** Baseline lab values with ALL of the following to demonstrate the diagnosis of XLH (i, ii, iii, iv, and v):
  - **(i)** Elevated serum intact Fibroblast Growth Factor 23 (e.g., greater than 22 pg/mL using Mayo assay, greater than 30 pg/mL using Kainos assay); AND
  - **(ii)** Normal serum calcium (e.g., 8.6 to 10.0 mg/dL for adults and 8.7 to 10.6 mg/dL for children); AND
  - **(iii)** Elevated serum alkaline phosphatase (e.g., Greater than 104 U/L for adults and greater than 335 U/L for children); AND
  - **(iv)** Low to normal 1,25 dihydroxyvitamin D levels (e.g., less than 86 pg/mL); AND
  - **(v)** Serum phosphorus is below normal range (e.g., Less than 2.5 mg/dL for adults and less than 4.3 mg/dL for children); AND

iii. Most recent renal function labs (within 90 days) show creatinine clearance (CrCl) is greater than or equal to 30 mL/min; AND

iv. Patient meets one of the following (1 or 2):
- **(1)** Patient has an intolerance, contraindication, or inadequate response to oral phosphate and vitamin D treatment for at least 6 months; OR
- **(2)** Patient is pediatric (aged 1–17 years) and has signs of rickets at the time of XLH diagnosis; AND

v. Oral phosphate and/or active vitamin D analogs are stopped at least 1 week prior to initiation of burosumab-twza; AND

vi. Documentation of clinical signs or symptoms of disease (e.g., rickets, growth retardation, musculoskeletal pain, bone fractures) for patients greater than or equal to 18 years old; AND

vii. Prescribed by or in consultation with a specialist experienced in the treatment of metabolic bone disorders.

B) Patients Currently Receiving Burosumab (Crysvita). Burosumab (Crysvita) may be approved for 1 year when ALL of the following are met (i, ii, iii, iv, and v):

i. Current serum phosphorous level (within 90 days) is below the upper limit of lab normal range (e.g., less than 4.5 mg/dL for adults and less than 5.4 mg/dL for children); AND

ii. Documented positive clinical response defined by any ONE of the following:
- **(1)** Increase in serum phosphorus levels (from baseline); OR

(2) Improvement in symptoms (e.g., skeletal pain, linear growth, improvement in skeletal deformities, reduction of fractures); OR
(3) Reduction in serum alkaline phosphatase activity from baseline; OR
(4) Improvement in radiographic imaging of rickets/osteomalacia; AND

iii. Client is not taking an oral phosphate; AND
iv. Client is not taking vitamin D; AND
v. Prescribed by or in consultation with a specialist experienced in the treatment of metabolic bone disorders.

Dosing. Approve one of the following dosing regimens (A, B, or C):

A) For adult patients (≥ 18 years of age), approve up to a maximum dose of 90 mg administered subcutaneously (SC) not more frequently than once every 4 weeks; OR
B) For pediatric patients 6 months or older, 10 kg or greater), approve up to a maximum dose of 2 mg/kg AND 90 mg administered SC not more frequently than once every 2 weeks.
C) For pediatric patients 6 months or older, less than 10 kg), approve up to a maximum dose of 2 mg/kg administered SC not more frequently than once every 2 weeks.

2. Tumor-Induced Osteomalacia (TIO). Approve Burosumab (Crysvita) for 1 year if the patient meets ONE of the following criteria (A or B):

A) Initial Therapy. Approve if the patient meets all of the following criteria (i, ii, iii, iv, v, vi, and vii):
i. The patient is ≥ 2 years of age; AND
ii. The medication is prescribed by or in consultation with an endocrinologist or nephrologist; AND
iii. The patient has a confirmed diagnosis of fibroblast growth factor 23 (FGF23)-related TIO that is not amendable to receive surgical excision of the offending tumor/lesion; AND
iv. The patient has a baseline serum phosphorus level that was below the normal range for age; AND
v. The patient has had a baseline (i.e., prior to any TIO treatment [e.g., Crysvita, oral phosphate/vitamin D]) tubular reabsorption of phosphate corrected for glomerular filtration rate (TmP/GFR) that was below the normal range for age and gender; AND
vi. An eGFR ≥ 30 mL/min/1.73 m^2; AND
vii. The patient meets ONE of the following (1 or 2):
(1) The patient has tried oral phosphate and calcitriol therapy for at least 6 months; OR

(2) Per the prescriber, the patient has a contraindication to oral phosphate therapy, calcitriol therapy, or both.

B) Patients Currently Receiving Burosumab (Crysvita). Approve if the patient is continuing to derive benefit from Burosumab (Crysvita) as determined by the prescriber.

Dosing. Approve one of the following dosing regimens (A or B):

A) For adult patients (≥ 18 years of age), approve up to a maximum dose of 2 mg/kg (not to exceed 180 mg) administered subcutaneously (SC) not more frequently than once every 2 weeks; OR

B) For pediatric patients (2 to 17 years of age), approve up to a maximum dose of 2 mg/kg (not to exceed 180 mg) administered subcutaneously (SC) not more frequently than once every 2 weeks.

Conditions Not Recommended for Approval

Burosumab (Crysvita) has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Chronic Kidney Disease (CKD), Severe Renal Impairment or End Stage Renal Disease**. Crysvita is contraindicated in patients with severe renal impairment or end stage renal disease (ESRD).[1] These patients often have abnormal mineral metabolism which may be associated with FGF23. However, Crysvita has not been studied for the treatment of patients with CKD who have elevations of FGF23 impacting phosphate regulation.[1,14]

2. **Epidermal Nevus Syndrome (ENS)**. A Phase II single-arm, open-label, dose-finding study (unpublished) included 16 adults with tumor induced osteomalacia (TIO) [n = 15] or ENS (n = 1) with hypophosphatemia and an elevated FGF23.[15] Crysvita Q4W improved mean serum phosphorus levels and increased markers of bone turnover (as measured by biopsy) at Weeks 16 and 24. More data are necessary to establish the efficacy and safety of Crysvita in patients with ENS.

Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Special Considerations

None.

Limitations/Exclusions

Please see link to member coverage documents below:

Line of Business	Link to Member Coverage Documents
Medicare Advantage Plans (Including D-SNP)	https://medicare.chpw.org/ Select the appropriate plan from the "Plans" drop down on the top navigation bar.
Apple Health Integrated Managed Care	https://www.chpw.org/for-members/benefits-and-coverage-imc/
Cascade Select	https://chnwhealthinsurance.chpw.org/member-center/plan-benefits/

List of Appendices

A. None.

Citations & References

CFR	42 CFR § 438.210	
WAC	WAC 284-43-2050	
RCW		
LOB & Contract Citation	☐ **WAHIMC**	
	☐ **BHSO**	
	☐ **Wraparound**	
	☐ **SMAC**	
	☐ **HH**	
	☐ **AHE**	
	☒ **MA/DSNP**	P&P supports all LOB requirements
	☒ **CS**	P&P supports all LOB requirements
Other Requirements		
NCQA Elements		
References	1. Crysvita® injection [prescribing information]. Novato, CA: Ultragenyx Pharmaceuticals Inc.; August 2025. 2. Carpenter TO, Imel EA, Holm IA, et al. A clinician's guide to x-linked hypophosphatemia. *J Bone Miner Res*. 2011;26(7):1381-1388.	

3. Scheinman S and Carpenter T. Hereditary hypophosphatemic rickets and tumor-induced osteomalacia. In: *UpToDate*, Sterns S and Geffner M (Ed), UpToDate. Waltham, MA. Accessed on April 20, 2023.
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8. Carpenter TO, Whyte MP, Imel EA, et al. Burosumab therapy in childre with X-linked hypophosphatemia. *N Engl J Med*. 2018;378(21):1987-199
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10. Insogna KL, Briot K, Imel EA, et al. A randomized, double-blind, placeb controlled, phase 3 trial evaluating the efficacy of burosumab, an ant FGF23 antibody, in adults with X-linked hypophosphatemia: week 2 primary analysis. *J Bone Miner Res*. 2018;33(8):1383-1393.
11. Portale AA, Carpenter TO, Brandi ML, et al. Continued beneficial effects of burosumab in adults with X-linked hypophosphatemia: results from a 24-week treatment continuation period after a 24-week double-blind placebo-controlled period. *Calcif Tissue Int.* 2019;105(3):271-284.
12. Imel EA, Glorieux FH, Whyte MP, et al. Burosumab versus conventional therapy in children with X-linked hypophosphataemia: a randomized, active-controlled, open-label, phase 3 trial. *Lancet*. 2019;393:2416-2427.
13. Dahir K, Zanchetta MB, Stanciu I, et al. Diagnosis and Management of Tumor-induced Osteomalacia: Perspectives from Clinical Experience. *J Endo Soc*. 2021;5(9):1-12.
14. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2020 April 8]. Available from: https://clinicaltrials.gov/ct2/results?cond=burosumab&term=&cntry=&state=&city=&dist=. Search terms: burosumab and KRN23.

15. Jan de Beur S, Miller PD, Weber TJ, et al. Effects of burosumab (KRN23), a human monoclonal antibody to FGF23, in patients with tumor-induced osteomalacia (TIO) or epidermal nevus syndrome (ENS) [poster SU0325]. Presented at: the American Society for Bone and Mineral Research (ASBMR) Annual Meeting; Denver, CO; September 9-11, 2017.
16. Haffner D, Emma F, Seefried L, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia. Nat Rev Nephrol. 2025 May;21(5):330-354.

OTHER REFERENCES UTILIZED

- Imel EA, Glorieux FH, Whyte MP, et al. Burosumab versus conventional therapy in children with X-linked hypophosphataemia: a randomized, active-controlled, open-label phase 3 trial. *Lancet*. 2019;393:2416-2427.
- Insogna KL, Rauch F, Kamenicky P, et al. Burosumab improved histomorphometric measures of osteomalacia in adults with X-linked hypophosphatemia: a phase 3, single-arm international trial. *J Bone Miner Res*. 2019;34(12):2183-2191.
- Washington State Healthcare Authority: Policy: Endocrine and Metabolic Agents: Metabolic Modifiers – X-Linked Hypophosphatemia (XLH) Agents burosumab-twza (Crysvita) Medical Policy No. 30.90.95-2 updated 8/10/20.

Revision History

Revision Date	Revision Description	Revision Made By
09/08/2020	New policy	Jennifer Farley, PharmD
10/12/2020	Approval	UM Committee
09/01/2021	Annual Review. Formatting Changes. Add background information regarding new indication for tumor-induced osteomalacia. Add new criteria for treatment of tumor-induced osteomalacia.	Alan Gabot, PharmD
09/28/2021	Approval	UM Pharmacy Subcommittee
07/06/2022	Annual Review. Updating criteria to match verbiage listed in HCA medical policy no. 30.90.95-2 for X-linked hypophosphatemia.	Alan Gabot, PharmD

07/07/2022	Approval	UM Pharmacy Subcommittee
05/03/2023	Annual Review. No criteria changes.	Alan Gabot, PharmD
05/04/2023	Approval	UM Pharmacy Subcommittee
03/12/2024	Annual Review. No criteria changes.	Alan Gabot, PharmD
03/13/2024	Approval	UM Criteria Subcommittee
01/08/2025	Annual Review. No criteria changes.	Alan Gabot, PharmD
01/08/2025	Approval	UM Criteria Subcommittee
11/03/2025	Annual Review. In background section, changed recommendations to reflect May 2025 XLH treatment guideline update. XLH Criteria updated to require either a trial/failure of phosphate and vitamin D OR symptomatic rickets in pediatric XLH patients.	Michael Tom, PharmD
11/14/2025	Approval	UM Criteria Subcommittee