IOWA | Health and Human Services

Crysvita (burosumab-twza)
PAM – 003

Iowa Medicaid Program	Prior Authorization	**Effective Date**	08/05/2019
Revision Number	7	**Last Reviewed**	04/18/2025
Reviewed By	Medicaid Medical Director	**Next Review**	04/17/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	11/02/2020

Overview

Medication: [1]	burosumab-twza
Brand Name:	Crysvita®
Pharmacologic Category:	Fibroblast growth factor 23 (FGF23) blocking antibody
FDA-Approved Indication(s):	1. Treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older. 2. Treatment of fibroblast growth factor 23 (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
How Supplied:	Single-dose vial: 10 mg/mL, 20 mg/mL, or 30 mg/mL
Dosage and Administration:	• Administered by subcutaneous injection (dosing in following table) • Should be administered by a healthcare provider • Stop oral phosphate and/or active vitamin D analogs 1 week prior to start of treatment
Benefit Category:	Medical

Dosage and Monitoring – **X-linked hypophosphatemia (XLH)**
Pediatric (6 months to less than 18 years of age) • Body weight < 10 kg: 1 mg/kg every 2 weeks (rounded to the nearest 1 mg) • Body weight ≥ 10 kg: 0.8 mg/kg every 2 weeks (rounded to the nearest 10 mg) ➢ Minimum starting dose: 10 mg ➢ Maximum dose (< 10 kg): 2 mg/kg (rounded to the nearest 1 mg) every 2 weeks ➢ Maximum dose (≥ 10 kg): 2 mg/kg, not to exceed 90 mg, every 2 weeks ➢ Measure fasting serum phosphorus every 4 weeks for the first 3 months, and thereafter as appropriate. ➢ Reassess fasting serum phosphorus level 4 weeks after any dose adjustment; do not adjust dose more frequently than every 4 weeks.
Adult (18 years of age and older) • 1 mg/kg body weight every 4 weeks (rounded to the nearest 10 mg) ➢ Maximum dose: 90 mg every 4 weeks ➢ Measure fasting serum phosphorus on a monthly basis (measured 2 weeks post-dose) for the first 3 months, and thereafter as appropriate. ➢ Reassess fasting serum phosphorus level 2 weeks after any dose adjustment; do not adjust dose more frequently than every 4 weeks.

Dosage and Monitoring – **Tumor-induced osteomalacia (TIO)**
Pediatric (2 years to less than 18 years of age) • 0.4 mg/kg body weight every 2 weeks (rounded to the nearest 10 mg) ➢ Maximum dose: 2 mg/kg, not to exceed 180 mg, every 2 weeks ➢ Measure fasting serum phosphorus on a monthly basis (measured 2 weeks post-dose) for the first 3 months, and thereafter as appropriate. ➢ Reassess fasting serum phosphorus level 4 weeks after any dose adjustment; do not adjust dose more frequently than every 4 weeks.
Adult (18 years of age and older) • 0.5 mg/kg body weight every 4 weeks (rounded to the nearest 10 mg) ➢ Maximum dose: 2 mg/kg, not to exceed 180 mg, every 2 weeks ➢ Measure fasting serum phosphorus on a monthly basis (measured 2 weeks post-dose) for the first 3 months, and thereafter as appropriate. ➢ Reassess fasting serum phosphorus level 2 weeks after any dose adjustment; do not adjust dose more frequently than every 4 weeks.

Descriptive Narrative

X-linked hypophosphatemia (XLH) is an inherited disorder characterized by low levels of phosphate in the blood (phosphate is abnormally processed by the kidneys, causing a loss of phosphate in the urine and leading to soft, weak bones [rickets]). The disorder is typically diagnosed in childhood and characteristic features include bowed or bent legs, short stature, bone pain, and severe dental pain. XLH is caused by mutations in the *PHEX* gene, leading to an increased concentration of fibroblast growth factor 23 (FGF23). This reduces the amount of phosphate reabsorbed by the kidneys, leading to hypophosphatemia and the resulting symptoms of XLH.[2]

The goal of therapy in children with XLH is to decrease the severity of the bone abnormalities (rickets and osteomalacia), improve growth and physical activity, and reduce associated bone/joint pain. Once a patient has reached adult height and the epiphyses have fused, treatment can still be of significant benefit, as hypophosphatemia may contribute to bone and joint pain, failure to heal fractures, and other symptoms such as muscle weakness and poor stamina.

Tumor-induced osteomalacia (TIO) (oncogenic osteomalacia) is characterized by the development of a tumor that causes the bones to be weakened. This occurs when a tumor secretes fibroblast growth factor 23 (FGF23), which inhibits the ability of the kidneys to absorb phosphate. The resulting hypophosphatemia causes rickets, osteomalacia, bone pain, muscle weakness, and fractures. Although primarily described in adults, TIO can occur in children and adolescents. Children with TIO present with clinical features of rickets, including gait disturbances, growth retardation, and skeletal deformities. The biochemical hallmarks of TIO are low serum phosphate levels, phosphaturia, and low or inappropriately normal levels of serum calcitriol.

Definitive treatment for TIO is complete tumor resection, which leads to prompt reversal of the biochemical abnormalities and healing of the bone disease over a period of 6 to 12 weeks. However, if the tumor is not localized, identified, and removed, medical management is required indefinitely, and Crysvita® is the preferred form of therapy. [3,4]

Guidelines

Clinical practice consensus for the diagnosis and management of X-linked hypophosphatemia (XLH) recommends Crysvita® in children in the following situations:

1. Radiographic evidence of overt bone disease and disease that is refractory to conventional therapy; or
2. Complications related to conventional therapy; or
3. Patient is unable to adhere to conventional therapy (presuming that adequate monitoring is feasible).[5]

For tumor-induced osteomalacia (TIO), curative treatment is by complete resection of the culprit tumor. If the tumor cannot be completely resected or cannot be localized, treatment with Crysvita® is preferred over treatment with phosphate and calcitriol.

Criteria

Prior authorization is required.

X-Linked Hypophosphatemia (XLH)

Crysvita® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of X-linked hypophosphatemia (XLH) is confirmed by **AT LEAST ONE** of the following;
    a. Genetic testing (in the member or a directly-related family member) confirms a mutation in the *PHEX* gene; **AND/OR**
    b. Elevated serum fibroblast growth factor 23 (FGF23) levels; **AND**
2. Member is 6 months of age or older; **AND**
3. Current serum phosphate level (within the last 30 days) is below the reference range for age and gender; **AND**
4. If member is 18 years of age or older *(if under age 18, move to criteria 5)*: has clinical signs and symptoms of XLH, including, but not limited to, bone pain, fractures, or limited mobility; **AND**
5. Prescribed by, or in consultation with, an endocrinologist or metabolic disease specialist; **AND**
6. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed (i or ii):
        i. Age 6 months to less than 18 years: 2 mg/kg (up to 90 mg) every 2 weeks; or
        ii. Age 18 years and older: 1 mg/kg (up to 90 mg) every 4 weeks; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Crysvita® is considered medically necessary for continuation of therapy in X-linked hypophosphatemia (XLH) when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation that member has experienced a positive clinical benefit to treatment with Crysvita® as evidenced by **BOTH** of the following:
    a. Member has achieved and sustained a clinically significant improvement in serum phosphate level; **AND**
    b. Demonstrated improvement and/or stabilization (upon subsequent renewals) in clinical signs or symptoms of X-linked hypophosphatemia (XLH) (e.g., enhanced height velocity, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain); **AND**
3. Prescribed by, or in consultation with, an endocrinologist or metabolic disease specialist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed (i or ii):
        i. Age 6 months to less than 18 years: 2 mg/kg (up to 90 mg) every 2 weeks; or
        ii. Age 18 years and older: 1 mg/kg (up to 90 mg) every 4 weeks; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Tumor-Induced Osteomalacia (TIO)

Crysvita® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of tumor-induced osteomalacia (TIO) confirmed by at least one of the following:
    a. Functional imaging (fluorodeoxyglucose-positron emission tomography [FDG-PET]/ computed tomography [CT], and Octreoscan/CT); and/or
    b. Anatomical imaging magnetic resonance imaging (MRI) and/or CT; and/or
    c. Venous sampling; **AND**
2. Member is 2 years of age or older; **AND**
3. Tumor(s) cannot be curatively resected or localized; **AND**
4. Serum fibroblast growth factor 23 level is greater than 100 pg/mL; **AND**
5. Serum phosphorus is below the normal range for age; **AND**
6. Member has clinical signs and/or symptoms of the disease including, but not limited to rickets, growth retardation, musculoskeletal pain, and/or bone fractures; **AND**
7. Prescribed by, or in consultation with, an endocrinologist or metabolic disease specialist; **AND**
8. Regimen prescribed meets one of the following (a or b):
    a. Does not exceed 2 mg/kg (up to 180 mg) every 2 weeks; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Crysvita® is considered medically necessary for continuation of therapy in tumor-induced osteomalacia (TIO) when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation that member has experienced a positive clinical benefit to therapy with Crysvita® as evidenced by:
   a. Member has achieved and sustained a clinically significant improvement in serum phosphate levels while on therapy; **AND**
   b. Demonstrated improvement and/or stabilization (upon subsequent renewals) in clinical signs or symptoms of TIO (e.g., enhanced height velocity, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain, and/or enhanced mobility); **AND**
3. Prescribed by, or in consultation with, an endocrinologist or metabolic disease specialist; **AND**
4. Regimen prescribed meets one of the following (a or b):
   a. Does not exceed 2 mg/kg (up to 180 mg) every 2 weeks; or
   b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Reference Ranges

Serum Phosphorus Levels (age & gender ranges) *†

Gender	Age	Serum Phosphorus[6]
Female	1 – 7 years	4.3 – 5.4 mg/dL
	8 – 13 years	4.0 – 5.2 mg/dL
	14 – 15 years	3.5 – 4.9 mg/dL
	16 – 17 years	3.1 – 4.7 mg/dL
	18+ years	2.5 – 4.5 mg/dL
Male	1 – 4 years	4.3 – 5.4 mg/dL
	5 – 13 years	3.7 – 5.4 mg/dL
	14 – 15 years	3.5 – 5.3 mg/dL
	16 – 17 years	3.1 – 4.7 mg/dL
	18+ years	2.5 – 4.5 mg/dL

Fibroblast Growth Factor 23 (FGF23) Levels*

Age	Intact FGF23, serum[7]
Pediatric (< 18 years)	≤ 52 pg/mL
Adult (18+ years)	≤ 59 pg/mL

* May be reduced in the absence of laboratory-specific ranges

† Note that reference values for serum phosphorus levels have not been established for patients younger than 12 months of age.

Approval Duration and Quantity Limits

	X-Linked Hypophosphatemia (XLH)		Tumor-Induced Osteomalacia (TIO)
	Pediatric (< 18 years)	Adult (18+ years)	
Quantity Limits	2 mg/kg every 2 weeks; maximum dose: 90 mg	1 mg/kg every 4 weeks; maximum dose: 90 mg	2 mg/kg every 2 weeks; maximum dose: 180 mg
Approval Duration	12 months (same for initial and subsequent prior authorizations on all indications)		

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J0584	Injection, burosumab-twza, 1 mg

ICD-10	Description
E83.30	Disorder of phosphorus metabolism, unspecified
E83.31	Familial hypophosphatemia
E83.39	Other disorders of phosphorus metabolism
M83.8	Other adult osteomalacia

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
42747-0102-01 (10 mg/mL)	Kyowa Kirin, Inc. (42747)	1 mg	1	EA	10
42747-0203-01 (20 mg/mL)	Kyowa Kirin, Inc. (42747)	1 mg	1	EA	20
42747-0304-01 (30 mg/mL)	Kyowa Kirin, Inc. (42747)	1 mg	1	EA	30

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Crysvita® prescribing information (03/2023). Kyowa Kirin, Inc.: Princeton, NJ. Available online: www.crysvitahcp.com. Accessed February 24, 2025.

[2] NIH: Genetics and Rare Diseases Information Center. X-linked dominant hypophosphatemic rickets. Available online at rarediseases.info.nih.gov. Accessed February 24, 2025.

[3] Scheinman SJ, Carpenter T. Hereditary hypophosphatemic rickets and tumor-induced osteomalacia. Kremen J, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed February 24, 2025.

[4] NIH: Genetics and Rare Diseases Information Center. Oncogenic osteomalacia. Available online at rarediseases.info.nih.gov. Accessed February 24, 2025.

[5] Haffner, D., Emma, F., Eastwood, D.M. *et al.* Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia. *Nat Rev Nephrol* 15, 435–455 (2019). Available online at www.nature.com/articles/s41581-019-0152-5.

[6] Phosphorus (Inorganic), Serum (Test ID: PHOS). Mayo Clinic Laboratories. Information available online at www.mayocliniclabs.com. Accessed February 24, 2025.

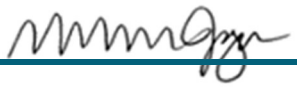
[7] Intact Fibroblast Growth Factor 23, Serum (Test ID: IFG23). Mayo Clinic Laboratories. Information available online at www.mayocliniclabs.com. Accessed February 24, 2025.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

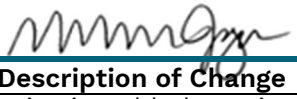
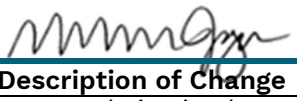
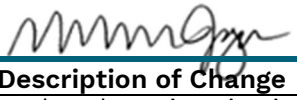
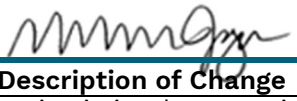
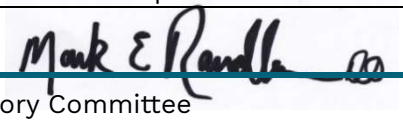
Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
04/18/2025	CAC	Annual review. Updated references.	7
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/19/2024	CAC	Annual review. Added dosing into criteria.	6
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
07/21/2023	CAC	Annual review. Updated labeler from Ultragenyx to Kyowa Kirin.	5
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/15/2022	CAC	Criteria: added requirement for serum phosphate level to have been drawn in the past 30 days. Formatting.	4
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/16/2021	CAC	Content/criteria changes (formatting).	3
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/17/2020	Medical Director	Updated age in criterion #2 under initial therapy criteria. Changed dosing to follow FDA labeling guidelines.	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
08/05/2019	Medical Director	Criteria implementation.	1
Signature Mark D. Randleman, DO			

CAC = Medicaid Clinical Advisory Committee