Crysvita (Burosumab-twza)
Policy Number: C14517A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
3/1/2016	03/28/2019	03/28/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL**
J0584 Inj, burosumab-twza1 mg	RxPA	Q2 2019

PRODUCTS AFFECTED: Crysvita (Burosumab-twza)

DRUG CLASS:
X-Linked Hypophosphatemia (XLH) Treatment - Agents

ROUTE OF ADMINISTRATION:
Subcutaneous injection by a healthcare provider

PLACE OF SERVICE:
Specialty Pharmacy or Buy and Bill

AVAILABLE DOSAGE FORMS:
Available as: 10 mg/mL, 20 mg/mL, or 30 mg/mL single-dose vials

FDA-APPROVED USES: Treatment of X-linked hypophosphatemia (XLH) in children ≥1 year and adults

COMPENDIAL APPROVED OFF-LABELED USES: None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: X-linked hypophosphatemia (XLH)

REQUIRED MEDICAL INFORMATION:

A. X-LINKED HYPOPHOSPHATEMIA:

1. Diagnosis of X-linked hypophosphatemia (XLH) as evidenced by: 1) Genetic/laboratory results (genetic testing or elevated serum fibroblast growth factor 23 level > 30pg/mL) 2) Clinical signs/symptoms (bone and joint pain, impaired physical function/gait disturbances, dental abnormalities, family history of XLH, waddling gait, hearing loss, or evidence of calcification of tendons, ligaments and joint capsules) and 3) Radiographic features (Radiographic evidence of active bone disease including rickets in the wrists and/or knees, femoral/tibial bowing, progressive bowing deformities of lower extremities, antero-medial rotational torsion of tibia, short stature, a Rickets Severity Score (RSS) score in the knee of at least 1.5 as determined by central read or osteomalacia-associated bone disease, stress fractures of lower extremities, pseudofractures, short stature, bowed legs)
   AND
2. Documentation of the following laboratory data: baseline serum phosphorus level below normal range for age and baseline tubular reabsorption of phosphorus corrected for glomerular filtration rate (TmP/GFR) below the normal range for age and gender
   AND

3. In patients that do NOT have documentation of the following symptoms: bone and joint pain, failure to heal fractures, muscle weakness and poor stamina: Documentation of an inadequate response [low serum phosphate levels (age appropriate)] despite at least SIX months of maximally tolerated oral phosphate and vitamin D metabolite or analog (e.g. calcitriol, doxercalciferol, alfacalcidiol, and paricalcitol)

DURATION OF APPROVAL: Initial authorization: 3 months, Continuation of therapy 12 months

QUANTITY: 90 mg/dose every two weeks, and all of the following: 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 day

PRESCRIBER REQUIREMENTS: Prescribed by, or in consultation with an endocrinologist, nephrologist, rheumatologist, orthopedic or specialist experienced in the treatment of metabolic bone disorders. Submit consultation notes if applicable.
NOTE: Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually.

AGE RESTRICTIONS: 1 year of age and older

GENDER:
Male and female

CONTINUATION OF THERAPY:
A. X-LINKED HYPOPHOSPHATEMIA:
1. Adherence to therapy as verified by Prescriber and member's medication fill history (review Rx history for compliance), including: adherent to the prescribed medication regimen, tolerance to therapy and no severe adverse reactions or drug toxicity
AND
2. Documentation therapy has resulted in clinical improvement from baseline or from the previous authorization, including but not limited to: normalization of serum phosphate or maintenance of normal serum phosphorus levels as evidenced by lab results with reference range, Positive clinical response, or stability of clinical signs and symptoms (including but not limited to): enhanced height velocity, enhanced mobility, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain, or clinical significant improvement from baseline in bone health

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION: All other uses of Crysvita (burosumab-twza) that are not an FDA-approved indication or not included in the 'Coverage Criteria' section of this policy are considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

OTHER SPECIAL CONSIDERATIONS: None

BACKGROUND:
X-linked hypophosphatemia (XLH)
Also called hereditary hypophosphatemic rickets; X-linked dominant hypophosphatemic rickets, X-linked vitamin D-resistant rickets). A rare, hereditary, progressive disorder caused by a mutation in the phosphate regulating endopeptidase (PHEX) gene. Characterized by renal phosphate wasting

due to an overproduction of fibroblast growth factor 23 (FGF23), a hormone that promotes urinary phosphate* excretion and suppresses renal production of active Vitamin D (1, 25 dihydroxy vitamin D) *Phosphate plays a critical role in the formation and growth of bones in childhood and helps maintain bone strength in adults; phosphate levels are controlled in large part by the kidneys. The kidneys normally rid the body of excess phosphate by excreting it in urine, and reabsorb phosphorus into the bloodstream when more is needed

Crysvita (burosumab-twza) binds to and inhibits the biological activity of FGF23 restoring renal phosphate reabsorption and increasing the serum concentration of 1, 25 dihydroxy vitamin D.

In pediatric patients, XLH results in rickets/osteomalacia that leads to lower-extremity deformities, slowed growth, dental abnormalities and reduced height. Adults with XLH experience osteomalacia and often have severe joint, bone and tooth pain and an increased incidence of stress fractures/pseudofractures, particularly in the lower extremities.

The most prevalent genetic form of rickets or osteomalacia; XLH affects an estimated 3,000 children and 12,000 adults in the United States (FDA 2018)

Current care options for XLH include supplements of multiple daily doses of phosphate and high-dose calcitriol (the active form of Vitamin D), growth hormones, corrective surgery, and dental treatment. The long-term outlook for patients with XLH varies depending on severity and whether complications arise.

APPENDIX:

Fasting serum phosphorus reference ranges for age (or as indicated by lab):

- 1 to 3 years: 3.8 to 6.5 mg/dL
- 4 to 11 years: 3.7 to 5.6 mg/dL
- 12 to 15 years: 2.9 to 5.4 mg/dL
- 16 to 19 years: 2.7 to 4.7 mg/dL

REFERENCES:

1. Crysvita [prescribing information]. Novato, CA: Ultragenyx Pharmaceutical; April 2018.
2. Carpenter TO, Whyte MP, Imel EA, Boot AM, Högler W, Linglart A, Padidela R, Van't Hoff W, Mao M, Chen CY, Skrinar A, Kakkis E, San Martin J, Portale AA. Burosumab Therapy in Children with X-Linked Hypophosphatemia. N Engl J Med. 2018 May 24;378(21):1987-1998. doi: 10.1056/NEJMoa1714641.
3. Munns CF, Shaw N, Kiely M, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. The Journal of Clinical Endocrinology and Metabolism. 2016;101(2):394-415. doi:10.1210/jc.2015-2175.
4. Ruppe MD. X-linked hypophosphatemia. GeneReviews. Available at: https://www.ncbi.nlm.nih.gov/books/NBK83985/. Updated April 13, 2017. Accessed on June 2018.
5. Ruppe MD, Zhang X , Imel EA , et al: Effect of four monthly doses of a human monoclonal anti-FGF23 antibody (KRN23) on quality of life in X-linked hypophosphatemia. Bone Rep 2016; 5:158-162.

6. Scheinman SJ, Drezner MK. Hereditary hypophosphatemia rickets and tumor-induced osteomalacia. UpToDate, Inc. Available at: www.uptodate.com. Updated September 26, 2017. Accessed on June 2018.
7. Ruppe MD. X-linked hypophosphatemia. GeneReviews. Available at: https://www.ncbi.nlm.nih.gov/books/NBK83985/. Updated April 13, 2017.