Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

Crysvita (burosumab-twza)

Policy Number: 5.01.660
Origination: 07/2018
Last Review: 07/2018
Next Review: 07/2019

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Crysvita (burosumab-twza) when it is determined to be medically necessary because the following criteria are met.

When Policy Topic is covered

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

FDA-Approved Indication

1. **X-Linked Hypophosphatemia (XLH).** Approve Crysvita if the patient meets the following criteria (A, B, and C):
   - **A)** The medication is prescribed by or in consultation with an endocrinologist or nephrologist; AND
   - **B)** The patient has had a baseline (i.e., prior to any XLH treatment [e.g., Crysvita, oral phosphate/vitamin D therapy]) serum phosphorus level that was below the normal range for age; AND
   - **C)** The patient has had a baseline (i.e., prior to any XLH 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.

   Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older.[1] In pivotal studies of Crysvita, patients had baseline serum phosphorus levels < the lower limit of normal for age.[1,6-14] Crysvita is contraindicated if the serum phosphorus is within or above the normal range for age.[1] Low serum phosphate levels and reduced tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR) are indicative of renal phosphate wasting and characteristic of XLH.[2-3]

   Crysvita is administered as a subcutaneous (SC) injection by a healthcare provider. It is given once every 2 weeks (Q2W) in pediatric patients 1 to < 18 years of age and once every 4 weeks (Q4W) in adult patients ≥ 18 years of age.

When Policy Topic is not covered

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 adult patients 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.

3. **Tumor-Induced Osteomalacia (TIO).** A Phase II single-arm, open-label, dose-finding study (unpublished) included 16 adult patients with 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 TIO.

Considerations

Crysvita requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service

Crysvita, a fibroblast growth factor 23 (FGF23) blocking antibody, is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients ≥ 1 year of age.[1] 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, Crysvita restores renal phosphate reabsorption and increases serum concentrations of 1,25 dihydroxyvitamin D. Crysvita is administered as a subcutaneous (SC) injection by a healthcare provider. It is given once every 2 weeks (Q2W) in pediatric patients 1 to < 18 years of age and once every 4 weeks (Q4W) in adult patients ≥ 18 years of age.

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, it 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. Current medical therapy for adults and children with XLH consists 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.

Rationale

Prior authorization is recommended for prescription benefit coverage of Crysvita. Because of the specialized skills required for evaluation and diagnosis of patients treated with Crysvita as well as the monitoring required for adverse events and long-term efficacy, approval requires Crysvita to be prescribed by or in consultation with a physician who specializes in the condition being treated.

References

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8. Carpenter T, Imel E, Boot A, et al. A randomized, open-label phase 2 study of KRN23, a fully human anti-FGF23 monoclonal antibody, in 52 children with x-linked hypophosphatemia (WLH): 40-week results [oral presentation 1154]. Presented at: the American Society for Bone and Mineral Research (ASBMR); Atlanta, GA; September 17-19, 2016.
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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); Denver, CO; September 9-11, 2017.

Other References Utilized:

- Carpenter T, Imel E, Linglart A, et al. Effects of burosumab (KRN23), a fully human anti-FGF23 monoclonal antibody, on functional outcomes in children with X-linked hypophosphatemia (XLH): final results from a randomized, 64-week, open-label phase 2 study [poster FR0331]. Presented at:

the American Society for Bone and Mineral Research (ASBMR); Denver, CO; September 9-11, 2017.
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Billing Coding/Physician Documentation Information

J3590 Crysvita is considered a medical benefit

Additional Policy Key Words

Policy Number: 5.01.660

Policy Implementation/Update Information

07/2018	New policy titled Crysvita (burosumab-twza)