Wellmark Advantage Health Plan

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Effective Date: 12/01/2022

Crysvita® (burosumab-twza)

HCPCS: J0584

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Diagnosis of X-linked hypophosphatemia (XLH) confirmed by:
      i. Genetic testing
      OR
      ii. Elevated serum fibroblast growth factor 23 (FGF23) level based on the normal range for age
      iii. Low serum phosphate level based on the normal range for age
      iv. Presence of clinical signs and symptoms of the disease (e.g. rickets, growth retardation, musculoskeletal pain, bone fractures)
   c. Diagnosis of FGF23-related hypophosphatemia in tumor induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be resected or localized confirmed by:
      i. Elevated FGF23 level based on the normal range for age
      ii. Low serum phosphate level based on the normal range for age
      iii. Low ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) based on the normal range for age
      iv. Presence of clinical signs and symptoms of the disease (e.g. bone pain, fractures, difficulty walking, muscle weakness and fatigue)
   d. Trial and failure, contraindication, or intolerance to active vitamin D and phosphate supplements
   e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in Wellmark Advantage Health Plan utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Initial Authorization Period: 6 months initially and annually thereafter
   c. Renewal Criteria: Clinical documentation showing improvement on therapy such as experienced normalization of serum phosphate and experienced a positive clinical response to burosumab (e.g.,

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enhanced height velocity, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain)

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Crysvita is a fibroblast growth factor 23 (FGF23) blocking antibody indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older and 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.

- XLH is a hereditary phosphate wasting condition, caused by inactivating mutations in the phosphate-regulating endopeptidase homolog X-linked (PHEX) gene. This leads to an increase in fibroblast growth factor 23 (FGF23 levels), which then causes renal wasting and decreased intestinal absorption of phosphate.

    - The diagnosis is confirmed with genetic testing for the PHEX mutation. However, genetic testing is not always necessary. For example, a patient with a family history consistent with the disease and biochemical features such as elevated FDF23 levels low and serum phosphate, and sign and symptoms consistent with the disease is sufficient to confirm the diagnosis and initiate treatment.

    - Skeletal abnormalities, including rickets, osteomalacia, and growth failure, are the major clinical findings in children with XLH. Although adults with XLH may have less obvious symptoms, they often have significant functional impairment and multiple complications, emphasizing that the disorder is truly lifelong and not simply a disorder of the growth plate that resolves with the cessation of growth.

- TIO is a rare, acquired paraneoplastic syndrome caused by tumoral overproduction of FGF23, which then causes renal wasting and decreased intestinal absorption of phosphate that acts primarily at the proximal renal tubule to inhibit phosphate reabsorption and 1α-hydroxylation of 25-hydroxyvitamin D, which leads to hypophosphatemia and eventually osteomalacia.

    - 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, the tumors that cause this syndrome are difficult to identify because they are small, slow growing, and may be found in bone or soft tissue anywhere in the body.

    - A diagnosis can be confirmed based on a combination of biochemical markers and history of clinical manifestations.

        - Biochemical markers which are consistent with the patient population from the clinical trial include

            - Elevated serum FGF23 level. The reference range can range based on the laboratory used. The majority of patients with tumor induced osteomalacia have FGF23 levels above 2 times the upper limit of the reference interval.

            - Low serum phosphorus level

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        - Low ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) <2.5 mg/dL. TmP/GFR provides the most accurate assessment of renal phosphate handling to confirm renal tubular phosphate wasting.

    - Signs and symptoms include bone pain, muscle pain, and fatigue.

    - Treatment of choice is resection of the tumor and is almost always curative and provides rapid improvement

- There are no established treatment guidelines for these conditions. The safety and efficacy of Crysvita was established based on clinical trials in patients with these conditions despite treatment with activated vitamin D and phosphate supplements. The standard of care when medical management is warranted, prior to the approval of Crysvita, was treatment with activated vitamin D and phosphate supplements as outlined in several published guidances. Activated vitamin D and phosphate supplements are effective treatment options and have shown to improve bone disease. There is insufficient evidence to establish that Crysvita is more effective than vitamin D and phosphate supplements at this time.

References:

1. Crysvita [prescribing information]. Novato, CA: Ultragenyx. June 2020.
2. Carpenter, TO, Imel, EA, Holm, IA, Jan de Beur, SM, Insogna, KL. A clinician's guide to X-linked hypophosphatemia. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2011 Jul;26(7):1381-8. PMID: 21538511.
3. Haffner D, Emma F, Eastwood DM, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia. Nat Rev Nephrol. 2019;15(7):435-455. doi:10.1038/s41581-019-0152-5
4. Florenzano P, Gafni RI, Collins MT. Tumor-induced osteomalacia. Bone Rep. 2017;7:90-97. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5633085/.
5. Marion DW. Pacing the diaphragm: Patient selection, evaluation, implantation, and complications. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on January 04, 2018.)
6. Hereditary hypophosphatemic rickets and tumor-induced osteomalacia
7. Scheinman SJ, Carpenter T, Drezner MK. Hereditary hypophosphatemia rickets and tumor-induced osteomalacia. UpToDate, Waltham, MA. (Accessed on July 6, 2018.)

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Policy History		
#	Date	Change Description
1.1	Effective Date: 12/01/2022	Annual review was completed, no changes to criteria
1.0	Effective Date: 01/01/2022	Effective date of policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

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