Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 12/12/2024

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 BCBSM/BCN 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., enhanced height velocity, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain)

***Note: Coverage and approval duration 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 FGF23 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

        - 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. Scheinman SJ, Carpenter T, Drezner MK. Hereditary hypophosphatemia rickets and tumor-induced osteomalacia. UpToDate, Waltham, MA. (Accessed on October 9, 2024.)

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.9</td><td>Effective Date:
12/12/2024</td><td>Annual review was completed, no changes to criteria</td></tr>
<tr><td>1.8</td><td>Effective Date:
12/14/2023</td><td>Annual review was completed, no changes to criteria</td></tr>
<tr><td>1.7</td><td>Effective Date:
12/01/2022</td><td>Annual review was completed, no changes to criteria</td></tr>
<tr><td>1.6</td><td>Effective Date:
12/09/2021</td><td>Removed physician requirement and the criteria requiring a score of 4 or greater on BPI question 3 for confirmation of XLH diagnosis.</td></tr>
<tr><td>1.5</td><td>Effective Date:
08/12/2021</td><td>Annual review was completed, no changes to criteria</td></tr>
<tr><td>1.4</td><td>Effective Date:
08/13/2020</td><td>Updates were made to the criteria, including adding criteria for a new indication</td></tr>
<tr><td>1.3</td><td>Effective Date:
12/05/2019</td><td>Updated for new FDA approved age</td></tr>
<tr><td>1.2</td><td>Effective Date:
10/01/2019</td><td>UM medical management system update for BCNA and MAPPO
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.1</td><td>Effective Date:
08/15/2019</td><td>Annual Review of Medical Policy</td></tr>
<tr><td>1.0</td><td>Effective Date:
08/09/2018</td><td>New full drug review
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
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** 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.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Crysvita® (burosumab-twza) HCPCS CODE: J0584

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This form is to be used by participating physicians to obtain coverage for Crysvita. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female **Pt weight (in kg)** **Date recorded:**_____	**Address**
Diagnosis	**City /State/Zip**
Drug Name ☐	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for initiation or renewal of therapy? ☐ Initiation ☐ Continuation ☐ *Date patient started therapy:* _____
2. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #3) *Reason for Hospital Outpatient administration:* _____
3. Please specify location of administration if hospital outpatient infusion: _____
4. Please provide the NPI number for the place of administration: _____
5. **Initiation AND Continuation of therapy:**
   a. Please check the patient's diagnosis:
      ☐ X-linked hypophosphatemia (XLH)
      ☐ Treatment of FGF23-related hypophosphatemia in tumor induced osteomalacia (TIO)
      ☐ Other: _____
   b. XLH:
      i. Genetic testing to confirm diagnosis: _____ ***(Please attach any tests confirming diagnosis)***
      ii. Please provide serum fibroblast growth factor 23 (FGF23) level: _____ Date: _____
      iii. Please provide the serum Phosphorus level in mg/dL: _____ Date: _____
      iv. Please provide the measurable bone/joint pain (BPI-Q3 score): _____ Date: _____
      v. What is the patient clinical signs and symptoms of the disease? ☐ Rickets ☐ Growth retardation ☐ Musculoskeletal pain ☐ Bone fractures ☐ Other: _____
   c. Is the FGF23-related hypophosphatemia in TIO associated with phosphaturic mesenchymal tumors that cannot be resected or localized?
      ☐ Yes ☐ No Comment: _____
      i. Please provide serum fibroblast growth factor 23 (FGF23) level: _____ Date: _____
      ii. Please provide the serum phosphorus level in mg/dL: _____ Date: _____
      iii. Please provide the ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR): _____ Date: _____ Normal reference range: _____
      iv. What is the patient clinical signs and symptoms of the disease? ☐ Bone pain ☐ Fractures ☐ Difficulty walking ☐ Muscle weakness ☐ Fatigue ☐ Other: _____
   d. Please select which drugs has the patient tried and failed for the requested indication: _____
      ☐ Vitamin D ☐ Phosphate supplements ☐ Other: _____
6. **Continuation request:** Crysvita start date: _____
   a. Has the patient had documented beneficial clinical response to Crysvita?
      ☐ Yes ☐ No Comment: _____
   b. How has the patient improved on therapy? ☐ Normalization of serum phosphate ☐ Enhanced height velocity ☐ Improvement in skeletal deformities ☐ Reduction of fractures ☐ Reduction of generalized bone pain ☐ Other: _____ ☐ None
7. *Please add any other supporting medical information necessary for our review*

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached Chart Notes	☐ Serum Pi level
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

5/9/2018;10/11/2018,11/20/2018; 10/1/2020