Burosumab-twza (Crysvita®)

NDC CODE(S) 69794-0102-XX CRYSVITA 10MG/ML Solution (ULTRAGENYX PHARMACEUTICAL)
69794-0203-XX CRYSVITA 20MG/ML Solution (ULTRAGENYX PHARMACEUTICAL)
69794-0304-XX CRYSVITA 30MG/ML Solution (ULTRAGENYX PHARMACEUTICAL)

DESCRIPTION

Burosumab-twza is a human immunoglobulin G subclass 1 (IgG1), anti-human fibroblast growth factor 23 (FGF23) antibody produced by recombinant DNA technology using Chinese hamster ovary cells. It was developed to treat a rare disease, X-linked hypophosphatemia (XLH). XLH is a rare, inherited form of rickets which causes low levels of phosphorus in the blood leading to impaired bone growth and development in children and adolescents as well as lifelong bone mineralization problems.

XLH differs from other forms of rickets in that standard vitamin D therapy is not effective treatment. XLH is caused by excess fibroblast growth factor 23 (FGF23) which suppresses renal tubular phosphate reabsorption and the renal production of 1,25 dihydroxy vitamin D. 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.

On June 18, 2020 it was also approved for the treatment of Tumor-Induced Osteomalacia associated with phosphaturic mesenchymal tumors, another condition caused by excessive FGF23,

POLICY

- Burosumab-twza for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**:
  - X-linked hypophosphatemia (XLH)
  - Tumor-Induced Osteomalacia
- Burosumab-twza for the treatment of other conditions/diseases is considered ***investigational***.

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient has not received oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) within 1 week prior to the start of therapy; **AND**
- Baseline fasting serum phosphorus* level with current hypophosphatemia, defined as a phosphate level below the lower limit of the laboratory normal reference range *(Note: serum phosphorus levels should be monitored periodically throughout therapy, required on renewal)*; **AND**
- Other causes of hypophosphatemia (e.g., autosomal dominant or recessive hypophosphatemic rickets) have been ruled out; **AND**

Universal Criteria

- Will not be used concomitantly with oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol); **AND**
- Patient has a reduced tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR); AND

- Patient does not have severe renal impairment, defined as a glomerular filtration rate (GFR) of <30 mL/min; **AND**
- Patient 25-hydroxy vitamin D levels will be monitored at baseline and intermittently and patient will be supplemented with cholecalciferol or ergocalciferol to maintain levels in the normal range for age; **AND**

X-linked Hypophosphatemia (XLH)

- Patient is at least 6 months of age; **AND**
- Diagnosis is confirmed by identifying at least one of the following:
  - Serum fibroblast growth factor-23 (FGF23) level > 30 pg/mL (>230 RU/mL in children 3 months-17 years; >180 RU/mL in adults using EDTA plasma); **OR**
  - Phosphate regulating gene with homology to endopeptidases located on the X chromosome (PHEX-gene) mutations in the patient; **AND**
- Adult patients must have had an inadequate response from oral phosphate and active vitamin D analogs

Tumor-induced Osteomalacia (TIO)

- Patient is at least 2 years of age; **AND**
- Must have a diagnosis of tumor-induced osteomalacia associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized; **AND**
- Diagnosis is confirmed by identifying excessive FGF23 (i.e., level ≥ 100 pg/mL) that is not amenable to cure by surgical excision of the offending tumor/lesion.

**Note: Phosphorous levels should be obtained fasting 12 hours or more without food or drink except for water and after an adequate washout period after supplements; lab values (i.e. GFR, phosphorous, TmP/GFR) should be obtained within 28 days of the date of administration.*

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria as identified in the Initial Approval Criteria; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe hypersensitivity reactions, hyperphosphatemia and/or nephrocalcinosis, severe injection site reactions, etc.; **AND**
- Current serum phosphorus level is not above the upper limit of the laboratory normal reference range; **AND**
- Disease response as indicated by increased serum phosphorus levels, a reduction in serum total alkaline phosphatase activity, improvement in symptoms (e.g., skeletal pain, linear growth, etc.), and/or improvement in radiographic imaging of Rickets/osteomalacia; **AND**
- Pediatric patients must be re-evaluated at adulthood or upon closure of bony epiphyses (whichever occurs first) in order to determine if continued therapy is necessary (i.e., discontinuation of burosumab in order to reassess whether treatment with oral phosphate and active vitamin D analogs provide an adequate response); **AND**
- *(Tumor-Induced Osteomalacia only):* If a patient undergoes treatment of the underlying tumor (i.e., surgical excision or radiation therapy) treatment should be interrupted, and serum phosphorus reassessed after treatment has been completed.

DOSAGE/ADMINISTRATION

INDICATION(S)	DOSAGE & ADMINISTRATION
X-linked	**Pediatrics*** **Weight <10 kg:**

hypophosphatemia (XLH)	• Starting dose is 1 mg/kg of body weight, rounded to the nearest 1 mg, administered every two weeks. **Weight ≥10 kg** • Starting dose is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, administered every two weeks • The minimum starting dose is 10 mg up to 90 mg ▫ *Measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment, and thereafter as appropriate.* ▫ *If serum phosphorus is below the reference range for age, dose may be increased (please refer to prescribing information for stepwise dose increase schedule).* ▫ *If serum phosphorous is above 5 mg/dL, withhold treatment. Once serum phosphorus is below the reference range for age, treatment may be restarted (please refer to prescribing information for re-initiation dose schedule).* **Adults*** • Starting dose is 1 mg/kg body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, administered every four weeks. ▫ *Assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate.* ▫ *If serum phosphorus is above the normal range, withhold the next dose. Once serum phosphorus is below the normal range, treatment may be restarted (please refer to prescribing information for re-initiation dose schedule).*
Tumor-Induced Osteomalacia	**Pediatrics*** • Starting dose is 0.4 mg/kg of body weight, rounded to the nearest 10 mg, administered every two weeks, up to a maximum dose of 2 mg/kg not to exceed 180 mg administered every two weeks. ▫ *After initiation of treatment, assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate* ▫ *If serum phosphorus is within the reference range for age, continue with the same dose* ▫ *Reassess fasting serum phosphorus level 4 weeks after dose adjustment (please refer to prescribing information for stepwise dose increase and decrease schedule)* ▫ *If a patient undergoes treatment of the underlying tumor (i.e., surgical excision or radiation therapy), treatment should be interrupted and serum phosphorus reassessed after treatment has been completed. Dose should be restarted at the patient's initiation dose if serum phosphorus remains below the lower limit of normal (please refer to prescribing information for dose adjustment schedule)* **Adults*** • Starting dose is 0.5 mg/kg body weight, rounded to the nearest 10 mg up to a maximum dose of 180 mg, administered every 2 weeks. ▫ *After initiation of treatment with, assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate* ▫ *If serum phosphorus is within the normal range, continue with the same dose.* ▫ *If serum phosphorus is below the normal range, the dose should be titrated (please refer to prescribing information for stepwise dose –adjustment schedule)* ▫ *If a patient undergoes treatment of the underlying tumor (i.e., surgical excision or radiation therapy), treatment should be interrupted, and serum phosphorus reassessed after treatment has been completed. Dose should be restarted at the patient's initiation*

	dose if serum phosphorus remains below the lower limit of normal (please refer to prescribing information for dose adjustment schedule)
***Note:** Do not adjust the burosumab dose more frequently than every 4 weeks - refer to the package insert for dose adjustments. Crysvita must be administered via subcutaneous injection by a healthcare provider.*	

LENGTH OF AUTHORIZATION

Initial coverage will be provided for 6 months and may be renewed every 12 months thereafter.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

- **XLH**
  - 90 billable units every 14 days (pediatrics)
  - 90 billable units every 28 days (adults)
- **TIO**
  - 180 billable units every 14 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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EFFECTIVE DATE 8/31/2021

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