Effective Date: 12/2019
Reviewed: 9/2019, 6/2020, 1/2021, 5/2021, 4/2022, 3/2023, 12/2023, 01/2024 Pharmacy Scope: Medicaid **Medical Scope:** Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

SPECIALTY GUIDELINE MANAGEMENT

CRYSVITA (burosumab-twza)

POLICY

I. SUMMARY OF EVIDENCE

Crysvita (burosumab-twza) 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. Clinical trials evaluating Crysvita in patients with XLH have demonstrated significant improvements in serum phosphorus levels, renal tubular reabsorption of phosphate (TmP/GFR), and bone mineralization parameters compared to placebo or conventional therapy.

II. CRITERIA FOR INITIAL APPROVAL

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

X-linked hypophosphatemia
A 6-month authorization may be granted for treatment of X-linked hypophosphatemia (XLH) when all of the following criteria are met:

1. Diagnosis of XLH confirmed by at least one of the following:
   a. 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**
   b. Phosphate regulating gene with homology to endopeptidases located on the X chromosome (PHEX-gene) mutations in the patient
2. Member is at least 6 months of age.
3. Adult patients must have had an inadequate response from oral phosphate and active vitamin D analogs.
4. For adults, dose requested is 1 mg/kg, rounded to nearest 10mg, every 4 weeks and dose does not exceed 90mg [Member's weight and dose must be provided].
5. For pediatric members (less than 10 kg) , dose requested is 1mg/kg, rounded to nearest 1mg, every 2 weeks and dose does not exceed 2mg/kg [Member's weight and dose must be provided].
6. For pediatric members (10 kg or greater), dose requested is 0.8 mg/kg, rounded to nearest 10mg, every 2 weeks and dose does not exceed 90mg [Member's weight and dose must be provided].

.

7. 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)*.
8. Must be prescribed by, or in consultation with, a nephrologist or endocrinologist.
9. Will not be used concomitantly with oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol).
10. Patient has a reduced tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR).
11. Patient does not have severe renal impairment, defined as a glomerular filtration rate (GFR) of <30 mL/min.
12. Other causes of hypophosphatemia (e.g., autosomal dominant or recessive hypophosphatemic rickets) have been ruled out.
13. Patient's 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.

Tumor-induced Osteomalacia (TIO)
A 6-month authorization may be granted for treatment of Tumor-induced Osteomalacia when all of the following criteria are met:

1. Must be prescribed by, or in consultation with, a nephrologist or endocrinologist.
2. Will not be used concomitantly with oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol).
3. Patient has a reduced tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR).
4. Patient does not have severe renal impairment, defined as a glomerular filtration rate (GFR) of <30 mL/min.
5. Patient's 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.
6. Patient is at least 2 years of age.
7. Must have a diagnosis of tumor-induced osteomalacia associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized.
8. 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.
9. 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)*.

.

10. Other causes of hypophosphatemia (e.g., autosomal dominant or recessive hypophosphatemic rickets) have been ruled out.
11. For adults, dose requested is 0.5 mg/kg, rounded to nearest 10mg; up to a maximum dose of 180mg every 2 weeks, [Member's weight and dose must be provided].
12. For pediatric members, dose requested is 0.4 mg/kg, rounded to nearest 10mg; up to a maximum dose of 180mg every 2 weeks, [Member's weight and dose must be provided].

**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.*

III. CONTINUATION OF THERAPY

A 12-month authorization may be granted to:

1. Patient continues to meet universal and other indication-specific relevant criteria as identified in section I.
2. 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.
3. Current serum phosphorus level is not above the upper limit of the laboratory normal reference range.
4. 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.
5. 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).
6. TIO only:
    a. 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.
    b. For adults, dose requested is 0.5 mg/kg, rounded to nearest 10mg; up to a maximum dose of 180mg every 2 weeks, [Member's weight and dose must be provided].

c. For pediatric members, dose requested is 0.4 mg/kg, rounded to nearest 10mg; up to a maximum dose of 180mg every 2 weeks, [Member's weight and dose must be provided].

7. XLH only:
   a. For adults with XLH, dose requested is 1 mg/kg, rounded to nearest 10mg, every 4 weeks and dose does not exceed 90mg [Member's weight and dose must be provided].
   b. For pediatric members (less than 10 kg) with XLH , dose requested is 1mg/kg, rounded to nearest 1mg, every 2 weeks and dose does not exceed 2mg/kg [Member's weight and dose must be provided].
   c. For pediatric members(10 kg or greater) with XLH, dose requested is up to 2mg/kg, rounded to nearest 10mg, every 2 weeks and dose does not exceed 90mg [Member's weight and dose must be provided].

IV. QUANTITY LIMIT

Crysvita 10 mg/mL vial: 1 vial every 14 days (0.072 ml per day)
Crysvita 20 mg/mL vial: 9 vials every 14 days (0.65 ml per day)
Crysvita 30 mg/mL vial: 6 vials every 14 days (0.45 ml per day)

V. DOSING AND ADMINSITRATION

X-Linked Hypophosphatemia (XLH)	*Pediatrics** Weight <10 kg: • 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 a maximum dose of 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	<u>*Pediatrics**</u> •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)* <u>*Adults**</u> • 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 Crysvita 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.*	

VI. <u>Medical Maximum units (</u>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

VII. HCPCS code:

- J0584 – Injection, burosumab-twza 1 mg; 1 billable unit = 1 mg

Per §§ 42 CFR 422.101, this clinical medical policy only applies to INTEGRITY in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Crysvita was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Crysvita according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

VIII. REFERENCES

1. Crysvita [package insert]. Bedminster, NJ: Kyowa Kirin, Inc.; December 2022.
2. NIH. U.S. National Library of Medicine. ClinicalTrials.gov website. http://clinicaltrials.gov/ct2/show/NCT02163577. Accessed October 24, 2018.
3. NIH. U.S. National Library of Medicine. ClinicalTrials.gov website. http://clinicaltrials.gov/ct2/show/NCT02526160. Accessed October 24, 2018.

.