Clinical Policy Title:	burosumab-twza
Policy Number:	RxA.080
Drug(s) Applied:	Crysvita®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

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.
- 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
burosumab-twza (Crysvita®)	XLH	Pediatric XLH • Weight less than 10 kg: 1 mg/kg rounded to the nearest 1 mg, SC every two weeks • Weight 10 kg or greater: 0.8 mg/kg rounded to the nearest 10 mg, SC every two weeks Increase dose up to approximately 2 mg/kg, SC every two weeks to achieve normal serum phosphorus. Adult XLH: 1 mg/kg body weight rounded to the nearest 10 mg SC every four weeks. Burosumab-twza should only be administered by a healthcare professional.	Pediatric XLH: 90 mg every two weeks Adult XLH: 90 mg every four weeks
	TIO	Pediatric TIO: 0.4 mg/kg rounded to the nearest 10 mg, SC every two weeks. Dose may be increased up to 2 mg/kg, SC not to exceed 180 mg, administered every two weeks. Adult TIO: Starting dose is 0.5 mg/kg, SC every four weeks. Dose may be increased up to 2 mg/kg, SC not to exceed 180 mg, administered every two weeks.	Pediatric TIO: 180 mg every two weeks Adult TIO: 180 mg every two weeks

Dosage Forms

- Single- dose vials for injection: 10 mg/mL, 20 mg/mL, 30 mg/mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. X- Linked Hypophosphatemia (must meet all)**:**

1. Member has a diagnosis of XLH confirmed by one of the following (a, b, or c):
   a. Genetic testing confirms the presence of mutation(s) in the phosphate regulating gene with homology to endopeptidases located on the X chromosome (*PHEX*) gene;
   b. Elevated serum fibroblast growth factor 23 (FGF23) levels consistent with X-linked hypophosphatemia (e.g., greater than 30 pg/mL);
   c. Pre-treatment tubular reabsorption of phosphate corrected for glomerular filtration rate (TmP/GFR) below the normal range for age and gender;
2. Prescribed by or in consultation with an endocrinologist, geneticist, nephrologist, or metabolic disease specialist;
3. Member is 6 months of age or older;
4. Member has tried and failed oral phosphate and calcitriol, at maximally indicated doses for an adequate trial period, unless contraindicated or clinically significant adverse effects are experienced;
5. Current (within the last 30 days) serum phosphorus level (without any XLH treatment) is below the reference range for age and gender (*use laboratory-specific reference ranges, if available; otherwise, see Appendix D for ranges*);
6. Member has clinical signs and symptoms of XLH (e.g., rickets, growth impairment, musculoskeletal pain, muscle stiffness/weakness, impaired mobility, bone fractures);
7. Member has discontinued oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) one (1)-week prior to initiation of treatment;
8. Dose does not exceed 90 mg every two weeks (pediatrics) or 90 mg every four weeks (adults).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Tumor-induced osteomalacia (must meet all):

1. Member has a diagnosis of FGF23-related hypophosphatemia in TIO associated with a phosphaturic mesenchymal tumor that cannot be curatively resected or localized;
2. Prescribed by or in consultation with an endocrinologist, nephrologist, or metabolic disease specialist;
3. Member is 2 years of age or older;
4. Member has tried and failed oral phosphate and calcitriol, at maximally indicated doses for an adequate trial period, unless contraindicated or clinically significant adverse effects are experienced;
5. Current (within the last 30 days) serum phosphorus level (without any TIO treatment) is below the reference range for age and gender (*use laboratory-specific reference ranges if available; otherwise, see Appendix D for ranges*);
6. Member has clinical signs and symptoms of TIO (e.g., bone pain, impaired mobility, muscle weakness, fatigue);
7. Member has discontinued oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) one (1)-week prior to initiation of treatment;

8. Dose does not exceed 180 mg every two weeks (pediatrics) or 180 mg every four weeks;

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All indications in Section I (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by both of the following (a and b):
   a. An increase in serum phosphorus levels from baseline and/or maintenance within the normal range for age and gender, not to exceed the upper limit of that normal range (*use laboratory-specific reference ranges if available; otherwise, see Appendix D for ranges*);
   b. A positive clinical response including any of the following: enhanced height velocity, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain;
3. If request is for a dose increase, member meets one of the followings (a or b):
   a. For XLH: Dose does not exceed 90 mg every two weeks (pediatrics) or 90 mg every four weeks (adults).
   b. For TIO: Dose does not exceed 180 mg every two weeks (pediatrics) or 180 mg every four weeks;

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
FGF23: Fibroblast Growth Factor 23
SC: Subcutaneous/subcutaneously
TIO: Tumor Induced Osteomalacia
TmP/GFR: Tubular resorption of Phosphate for Glomerular Filtration Rate
XLH: X-Linked Hypophosphatemia

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Concomitant use with oral phosphates and active vitamin D analogs;
  - Initiation of burosumab-twza therapy when serum phosphorus is within or above the normal range for age;
  - Severe renal impairment or end stage renal disease because these conditions are associated with abnormal mineral metabolism.

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Laboratory-specific reference ranges for serum phosphorus levels should be used when available; otherwise, the age- and gender-based reference ranges found below may be used:

Females	Males
1-7 years of age: 4.3-5.4 mg/dL	1-4 years of age: 4.3-5.4 mg/dL
8-13 years of age: 4.0-5.2 mg/dL	5-13 years of age: 3.7-5.4 mg/dL
14-15 years of age: 3.5-4.9 mg/dL	14-15 years of age: 3.5-5.3 mg/dL
16-17 years of age: 3.1-4.7 mg/dL	16-17 years of age: 3.1-4.7 mg/dL
18 years of age and older: 2.5-4.5 mg/dL	18 years of age and older: 2.5-4.5 mg/dL

- Age-based normal tubular resorption of phosphate corrected for glomerular filtration rate (TmP/GFR) reference:

	Females	Males
Birth	3.6-8.6 mg/dL (1.43-3.43 mmol/L)	
3 months	3.7-8.25 mg/dL (1.28-3.3 mmol/L)	
6 months	2.9-6.5 mg/dL (1.15-2.6 mmol/L)	
2-15 years	2.9-6.5 mg/dL (1.15-2.6 mmol/L)	
25-35 years	2.4-3.6 mg/dL (0.96-1.44 mmol/L)	2.5-3.4 mg/dL (1-1.35 mmol/L)
45-55 years	2.2-3.6 mg/dL (0.88-1.42 mmol/L)	2.2-3.4 mg/dL (0.9-1.35 mmol/L)
65-75 years	2-3.4 mg/dL (0.8-1.35 mmol/L)	

- For pediatric patients continuing burosumab-twza therapy, if serum phosphorus is greater than 5 mg/dL, it is recommended to withhold the dose until the serum phosphorus level falls below the reference range per age.

- For adult patients continuing burosumab-twza therapy, if serum phosphorus is above the upper limit of the normal range, it is recommended to withhold the dose until the serum phosphorus level falls below the reference range.

References

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10. Ruppe MD. X-Linked Hypophosphatemia. 2012 Feb 9 [Updated 2017 Apr 13]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021. Table 2. [Age-Based Normal TmP/GFR Reference Intervals]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK83985/table/rickets-xlh.T.agebased_normal_tmpgfr_ref/

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
No changes	04/2020	05/2020
Policy reviewed and updated. 1. Clinical policy title and lines of business updated. 2. TIO indication, dosing, and criteria for approval added. 3. Initial criteria for approval and duration of approval updated. 4. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…". 5. References reviewed and updated.	02/08/2021	03/09/2021