Clinical Policy: Burosumab-twza (Crysvita)

Reference Number: CP.PHAR.11
Effective Date: 05.08.18
Last Review Date: 08.19
Line of Business: Commercial, Medicaid, HIM-Medical Benefit

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Burosumab-twza (Crysvita®) is a fibroblast growth factor 23 (FGF23) blocking antibody.

FDA Approved Indication(s)

Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Crysvita is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of XLH confirmed by one of the following (a or b):
   a. DNA testing confirms the presence of mutations in the *PHEX* gene;
   b. Elevated serum FGF23 levels;
2. Prescribed by or in consultation with an endocrinologist or metabolic disease specialist;
3. Age ≥ 1 year;
4. Current (within the last 30 days) serum phosphorus level is below the reference range for age and gender (*use laboratory-specific reference ranges if available; otherwise, see Appendix D for ranges*);
5. Presence of clinical signs and symptoms of the disease (e.g., rickets, growth impairment, musculoskeletal pain, bone fractures);
6. Dose does not exceed 90 mg every two weeks (pediatrics) or 90 mg every four weeks (adults).

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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, new dose does not exceed 90 mg every two weeks (pediatrics) or 90 mg every four weeks (adults).

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
FGF23: fibroblast growth factor 23
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 Crysvita 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: 4.3-5.4 mg/dL	1-4 years: 4.3-5.4 mg/dL
8-13 years: 4.0-5.2 mg/dL	5-13 years: 3.7-5.4 mg/dL
14-15 years: 3.5-4.9 mg/dL	14-15 years: 3.5-5.3 mg/dL
16-17 years: 3.1-4.7 mg/dL	16-17 years: 3.1-4.7 mg/dL
≥ 18 years: 2.5-4.5 mg/dL	≥ 18 years: 2.5-4.5 mg/dL

- For pediatric patients continuing on Crysvita therapy, if serum phosphorus is > 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 on Crysvita 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
XLH	**Pediatric XLH** 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. Crysvita should only be administered by a healthcare professional.	Pediatric XLH: 90 mg every two weeks Adult XLH: 90 mg every four weeks

VI. Product Availability

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

VII. References

1. Crysvita Prescribing Information. Novato, CA: Ultragenyx Pharmaceutical Inc; September 2018. Available at: www.crysvita.com. Accessed May 4, 2019.

2. Carpenter TO, et al. A clinician's guide to X-linked hypophosphatemia. JBMR 2011; 26(7):1381-8. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/jbmr.340.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0584	Injection, burosumab-twza, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	05.08.18	08.18
No significant changes: added HIM-Medical Benefit line of business per SDC.	10.23.18	
3Q 2019 annual review: removed the requirement for a prior trial of calcitriol plus oral phosphates based on updated clinical trial data demonstrating superiority of Crysvita over calcitriol plus oral phosphates; references reviewed and updated.	05.14.19	08.19

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to

applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.