Medical Policy:

Crysvita® (burosumab-twza) subcutaneous injection

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.307	March 26, 2025	2018

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Crysvita, a fibroblast growth factor 23 (FGF23) blocking antibody, is indicated for:

- **Tumor-induced osteomalacia**, for treatment of FGF-related hypophosphatemia associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in patients ≥ 2 years of age.
- **X-linked hypophosphatemia** in patients ≥ 6 months of age.

Length of Authorization

Tumor-induced osteomalacia- 6 months
X-linked hypophosphatemia- 12 months

Dosing Limits [Medical Benefit]

Quantity Limit (max daily dose) [NDC Unit]:

- Crysvita 10 mg/mL vial: 1 vial every 14 days
- Crysvita 20 mg/mL vial: 1 vial every 14 days
- Crysvita 30 mg/mL vial: 6 vials every 14 days

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

- X-linked hypophosphatemia
  - 90 billable units every 14 days
- Tumor-induced osteomalacia
  - 180 billable units every 14 days

Guideline

1. **Tumor-Induced Osteomalacia.** Approve Crysvita for the duration noted if the patient meets ONE of the following criteria (A or B):
   A. Initial Therapy. Approve for 6 months if the patient meets ALL of the following criteria (i, ii, iii, iv, v, vi, and vii):
      i. Patient is ≥ 2 years of age; **AND**
      ii. Patient has a mesenchymal tumor that cannot be curatively resected or identified/localized; **AND**
      iii. Patient is currently exhibiting one or more signs or symptoms of tumor-induced osteomalacia, as determined by the prescriber; **AND**
      Note: Examples of signs and symptoms of tumor-induced osteomalacia include bone pain, impaired mobility, muscle weakness, and fatigue.
      iv. Patient has had a baseline serum phosphorus level that was below the normal range for age; **AND**
      Note: "Baseline" is defined as prior to receiving any tumor-induced osteomalacia treatment, such as Crysvita, oral phosphate, or vitamin D therapy.
      v. Patient has had a baseline tubular reabsorption of phosphate corrected for glomerular filtration rate (TmP/GFR) that was below the normal range for age and gender; **AND**
      Note: "Baseline" is defined as prior to receiving any tumor-induced osteomalacia treatment, such as Crysvita, oral phosphate, or vitamin D therapy.
      vi. Patient meets ONE of the following (1 or 2):
         1. Patient has tried oral phosphate and calcitriol therapy; **OR**
         2. Per the prescriber the patient has a contraindication to oral phosphate therapy, calcitriol therapy, or both; **AND**
      vii. The medication is prescribed by, or in consultation with, an endocrinologist or nephrologist.
   B. Patient is Currently Receiving Crysvita. Approve for 1 year if the patient is continuing to derive benefit from Crysvita as determined by the prescriber.
      Note: Examples of a response to Crysvita therapy are increased phosphorus levels, decreased symptoms of bone pain and/or muscle weakness, and increased mobility.

2. **X-Linked Hypophosphatemia.** Approve Crysvita for the duration noted if the patient meets ONE of the following criteria (A or B):
   A. Initial Therapy. Approve for 1 year if the patient meets ALL of the following criteria (i, ii, iii, and iv):
      i. Patient has had a baseline serum phosphorus level that was below the normal range for age; **AND**
      Note: "Baseline" is defined as prior to receiving any X-linked hypophosphatemia treatment, such as Crysvita, oral phosphate, or vitamin D therapy.
      ii. Patient meets ONE of the following (a or b):

a. Patient has had a baseline tubular reabsorption of phosphate corrected for glomerular filtration rate (TmP/GFR) that was below the normal range for age and gender; **OR**
Note: "Baseline" is defined as prior to receiving any X-linked hypophosphatemia treatment, such as Crysvita, oral phosphate, or vitamin D therapy.
b. Patient has had a genetic test confirming the diagnosis of X-linked hypophosphatemia via identification of a PHEX pathogenic variant; **AND**

iii. If the patient is ≥ 18 years of age, the patient meets BOTH of the following (a and b):
a. Patient is currently exhibiting one or more signs or symptoms of X-linked hypophosphatemia, as determined by the prescriber; **AND**
Note: Examples of signs and symptoms of X-linked hypophosphatemia in patients ≥ 18 years of age include fractures/pseudofractures, bone and joint pain, muscle weakness, and impaired mobility.
b. Patient meets ONE of the following (1 or 2):
1. Patient has tried oral phosphate and calcitriol therapy; **OR**
2. Per the prescriber the patient has a contraindication to oral phosphate therapy, calcitriol therapy, or both; **AND**

iv. The medication is prescribed by, or in consultation with, an endocrinologist or nephrologist.

B. Patient is Currently Receiving Crysvita. Approve for 1 year if the patient is continuing to derive benefit from Crysvita as determined by the prescriber.
Note: Examples of a response to Crysvita therapy are increased phosphorus levels, radiographic improvement in deformities, healing of fractures/pseudofractures, reduction in the incidence of new fractures/pseudofractures.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Crysvita is not recommended in the following situations:

1. **Chronic Kidney Disease, Severe Renal Impairment or End Stage Renal Disease**. Crysvita is contraindicated in patients with severe renal impairment or end stage renal disease. These patients often have abnormal mineral metabolism which may be associated with FGF23. However, Crysvita has not been studied for the treatment of patients with chronic kidney disease who have elevations of FGF23 impacting phosphate regulation.

2. **Epidermal Nevus Syndrome (including Cutaneous Skeletal Hypophosphatemia Syndrome).** More data are necessary to establish the efficacy and safety of Crysvita in patients with epidermal nevus syndrome. Patients with epidermal nevus syndrome were eligible to enroll in one of the Phase II tumor-induced osteomalacia studies of Crysvita. However, no patients with epidermal nevus syndrome enrolled.

Applicable Procedure Codes

Code	Description
J0584	Crysvita 10mg/mL Solution, Injection, burosumab-twza 1 mg

Applicable NDCs

Code	Description
42747-0203-01	Crysvita 20mg/mL Solution, Injection, burosumab-twza 1 mg
42747-0102-01	Crysvita 10mg/mL Solution, Injection, burosumab-twza 1 mg

42747-0304-01	Crysvita 30mg/mL Solution, Injection, burosumab-twza 1 mg

ICD-10 Diagnoses

Code	Description
M83.8	Other adult osteomalacia
E83.31	Familial X-linked hypophosphatemia
E83.39	Other disorders of phosphorus metabolism

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	3/26/2025	Annual Review: X-Linked Hypophosphatemia: The term "mutation" was updated to "pathogenic variant".Conditions Not Recommended for Approval: Epidermal Nevus Syndrome was clarified to include Cutaneous Skeletal Hypophosphatemia Syndrome. Updated billable units and quantity limits
EmblemHealth & ConnectiCare	5/6/2024	Annual Review: Added E83.39, Removed the following statement: "Indications and/or approval conditions noted with [eviCore] are managed by eviCore healthcare for those clients who use eviCore for oncology and/or oncology-related reviews. For these conditions, a prior authorization review should be directed to eviCore at www.eviCore.com."
EmblemHealth & ConnectiCare	9/6/2023	Updated NDCs- removed: 69794-0203-01, 69794-0102-01 and 69794-0304-01. Added 42747-0102-01, 42747-0203-01, and 42747-0304-01.
EmblemHealth & ConnectiCare	4/4/2023	Transfer from CCUM Template to Medical CoBranded Template Retired MG.MM.PH.116
EmblemHealth & ConnectiCare	3/22/2022	Annual Revision: No Criteria Changes
EmblemHealth & ConnectiCare	6/9/2021	Annual Revision: No Criteria Changes

References

1. Crysvita® injection [prescribing information]. Novato, CA: Ultragenyx; June 2020.