CRYSVITA® (BUROSUMAB-TWZA)

Policy Number: CS2020D0071G
Effective Date: January 1, 2020

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APPLICATION

This policy does not apply to the states of Kansas, Louisiana, and Pennsylvania.
• For the state of Louisiana, refer to the Medical Benefit Drug Policy titled Crysvita® (Burosumab-Twza) (for Louisiana Only).
• For the state of Pennsylvania, refer to the Medical Benefit Drug Policy titled Crysvita® (Burosumab-Twza) (for Pennsylvania Only).

COVERAGE RATIONALE

Crysvita (burosumab) is proven and medically necessary for the treatment of X-linked hypophosphatemia (XLH) when the following criteria are met: 1
• For initial therapy, all of the following:
  o Diagnosis of XLH, confirmed by one of the following:
    ▪ Genetic testing (e.g., confirmed PHEX gene mutation in patient or first-degree relative)
    ▪ Elevated Serum fibroblast growth factor 23 (FGF23) level > 30 pg/mL;
    and
  o Patient is greater than 6 months of age; and
  o One of the following:
    ▪ Patient epiphyseal plate has not fused; or
    ▪ All of the following:
      - Patients’ epiphyseal plate has fused; and
      - Patient is experiencing clinical signs and symptoms of the disease (e.g., limited mobility, musculoskeletal pain, bone fractures); and
      - Failure, contraindication, or intolerance to therapy with calcitriol in combination with an oral phosphate agent (e.g., K-Phos®, K-Phos Neutra®);
    and
  o Prescribed by, or in consultation with, an endocrinologist or specialist experienced in the treatment of metabolic bone disorders; and
  o Fasting serum phosphorus is below the normal range for age; and
  o Dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  o Initial authorization will be for no more than 12 months
• For continuation therapy, all of the following:
  o Patient has previously received treatment with burosumab; and
  o Prescribed by, or in consultation with, an endocrinologist or specialist experienced in the treatment of metabolic bone disorders; and
  o Patient has experienced normalization of serum phosphate while on therapy; and
  o Patient has experienced a positive clinical response to burosumab (e.g., enhanced height velocity, improvement in skeletal deformities, reduction of fractures, reduction of generalized bone pain); and
XHL is a heritable disorder of renal phosphate transport, which results in abnormal phosphate hemostasis, resulting in hypophosphatemia and abnormal bone mineralization. Elevated serum FGF23 levels are observed in patients with XLH, and believed to be associated with phosphate level abnormalities. Burosumab inhibits excess FGF23 levels, which results in normalization of serum phosphate.\textsuperscript{1-3} Combining active vitamin D metabolites with a balanced dose of phosphate has been the mainstay of therapy for XHL. Most affected children are candidates for treatment. In adults, the role of treatment has not been well studied; treatment is generally reserved for individuals with symptoms such as skeletal pain, upcoming orthopedic surgery, biochemical evidence of osteomalacia with an elevated serum alkaline phosphatase (ALP) level, or recurrent pseudofractures or stress fractures. The primary goals of treatment in children are to correct or minimize rickets/osteomalacia, as assessed by radiographic abnormalities and resolution of skeletal abnormalities. In contrast with children, once a patient reaches adult height and the epiphyses have fused, the goal of therapy is simply to manage generalized bone pain and enhance limited mobility, if either occurs, and to cure any non-union fractures.\textsuperscript{5}

### CLINICAL EVIDENCE

A randomized, open-label study (NCT 02163577) in 52 prepubescent XLH patients compared burosumab administered every 2 weeks versus every 4 weeks. Upon completion of a 16-week dose titration, patients were administered burosumab every 2 weeks for 48 weeks. No study patients discontinued burosumab and completed at least 64 weeks of the study. Patient dosing was individualized to achieve a target fasting serum phosphorus concentration of 3.5 to 5.0 mg/dL based on the fasting phosphorus level the day of dosing. Twenty-six of 52 patients received burosumab every two weeks up to a maximum dose of 2 mg/kg. The average dose was 0.73 mg/kg (range: 0.3, 1.5) at week 16, 0.98 mg/kg (range: 0.4, 2.0) at week 40 and 1.04 mg/kg (range: 0.4, 2.0) at week 60. The other 26 patients received burosumab every four weeks. At the beginning of the study, the mean age of patients was 8.5 years with 46% male. Regarding treatment with oral phosphate and active vitamin D analogs, 96% of study participants had received these for a mean (SD) duration of 7 (2.4) years. In addition, discontinuation of oral phosphate and active vitamin D analogs occurred prior to study enrollment. Radiographic evidence of rickets was observed in 94% of patients at baseline. In this study, patients receiving burosumab experienced a mean (SD) increase in serum phosphorus levels from 2.4 (0.40) at baseline to 3.3 (0.40) and 3.4 (0.45) mg/dL at week 40 and week 64 in the patients who received burosumab every 2 weeks. The 10-point Thacher Rickets Severity Score (RSS) and the 7-point Radiographic Global Impression of Change (RGI-C) were used to evaluate rickets. After 40 weeks of therapy, mean total RSS decreased from 1.9 to 0.8 and the mean RGI-C Global score was +1.7 in patients receiving burosumab every two weeks. Eighteen out of 26 patients achieved an RGI-C score of ≥ +2.0. These findings were maintained at week 64.\textsuperscript{1,4}

A 64-week open-label study (NCT 02750618) was conducted in 13 XLH patients age 1 to 4 years old. Study patients received burosumab at a dose of 0.8 mg/kg every two weeks with titration up to 1.2 mg/kg based on serum phosphorus. No study participants discontinued burosumab. The mean age of patients was 2.9 years at study entry. At baseline, all study participants had radiographic evidence of rickets and had received oral phosphate and active vitamin D analogs for a mean (SD) duration of 16.9 (13.9) months. Discontinuation of oral phosphate and active vitamin D analogs occurred prior to study enrollment. At week 40, patients experienced an increased mean (SD) serum phosphorus levels from 2.5 (0.28) mg/dL at baseline to 3.5 (0.49) mg/dL. After 40 weeks of treatment, mean total RSS decreased from 2.9 to 1.2 and the mean (SE) RGI-C Global score was +2.3 (0.08). All 13 patients achieved

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**APPLICABLE CODES**

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

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<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tr>
<td>J0584</td>
<td>Injection, burosumab-twza, 1 mg</td>
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<table>
<thead>
<tr>
<th>ICD-10 Diagnosis Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>E83.31</td>
<td>Familial hypophosphatemia</td>
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</table>

**BACKGROUND**

XHL is a heritable disorder of renal phosphate transport, which results in abnormal phosphate hemostasis, resulting in hypophosphatemia and abnormal bone mineralization. Elevated serum FGF23 levels are observed in patients with XLH, and believed to be associated with phosphate level abnormalities. Burosumab inhibits excess FGF23 levels, which results in normalization of serum phosphate.\textsuperscript{1-3} Combining active vitamin D metabolites with a balanced dose of phosphate has been the mainstay of therapy for XHL. Most affected children are candidates for treatment. In adults, the role of treatment has not been well studied; treatment is generally reserved for individuals with symptoms such as skeletal pain, upcoming orthopedic surgery, biochemical evidence of osteomalacia with an elevated serum alkaline phosphatase (ALP) level, or recurrent pseudofractures or stress fractures. The primary goals of treatment in children are to correct or minimize rickets/osteomalacia, as assessed by radiographic abnormalities and resolution of skeletal abnormalities. In contrast with children, once a patient reaches adult height and the epiphyses have fused, the goal of therapy is simply to manage generalized bone pain and enhance limited mobility, if either occurs, and to cure any non-union fractures.\textsuperscript{5}

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a RGI-C global score ≥ +2.0. The mean (SE) lower limb deformity as assessed by RGI-C, using standing long leg radiographs, was +1.3 (0.14).1,5

A randomized, double-blind, placebo-controlled study (NCT 02526160) in 134 adult XLH patients was completed. Burosumab was administered at a dose of 1 mg/kg every 4 weeks. At study entry, the patient age ranged from 16 to 66 years, with a mean of 40 years. The average age of diagnosis was 9 years and 81% of patients had received conventional therapy before the age of 18, for an average of approximately 12 years. 69% of patients who received burosumab were not allowed during the study. After 48 weeks of treatment, healing of osteomalacia was observed in ten patients as demonstrated by decreases in Osteoid volume/Bone volume from a mean (SD) score of 26% (12.4) at baseline to 11% (6.5), a change of -57%. Osteoid thickness declined in eleven patients. Mineralization lag time (demonstrated by decreases in Osteoid volume/Bone volume from a mean (SD) score of 26% (12.4) at baseline to 11% (6.5), a change of -57%).

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.1

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for Crysvita® (burosumab-twza injection). Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 – Drugs and Biologicals.

(Accessed March 28, 2019)

REFERENCES


### POLICY HISTORY/REVISION INFORMATION

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
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<tr>
<td>01/01/2020</td>
<td>Added language to indicate this policy does not apply to the states of Louisiana and Pennsylvania:</td>
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#### Application
- Replaced medical necessity criterion for initial therapy requiring “patient is greater than 1 year of age” with “patient is greater than 6 months of age”

#### Coverage Rationale
- Updated FDA section to reflect the most current information
- Archived previous policy version CS2019D0071F

### INSTRUCTIONS FOR USE

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage.

UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies 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.