CRYSVITA® (BUROSUMAB-TWZA) (FOR LOUISIANA ONLY)

Policy Number: CSLA2019D0071F

Effective Date: June 1, 2019

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APPLICATION

This Medical Benefit Drug Policy only applies to the state of Louisiana.

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:
  - 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;
  - Patient is greater than 1 year of age; and
  - 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®);
  - Prescribed by, or in consultation with, an endocrinologist or specialist experienced in the treatment of metabolic bone disorders; and
  - Fasting serum phosphorus is below the normal range for age; and
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  - Initial authorization will be for no more than 12 months.

- For continuation therapy, all of the following:
  - Patient has previously received treatment with burosumab; and
  - Prescribed by, or in consultation with, an endocrinologist or specialist experienced in the treatment of metabolic bone disorders; and
  - Patient has experienced normalization of serum phosphate while on therapy; and
  - 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
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  - Reauthorization will be for no more than 12 months.
###背景

XLH是一种先天性佝偻病，导致异常的磷酸盐平衡和骨矿化异常。升高血浆FGF23水平在XLH患者中被观察到，也与磷酸盐水平异常有关。Burosumab抑制过高的FGF23水平，结合活性维生素D代谢物与平衡磷酸盐水平的治疗已成为XLH的主要治疗方法。大多数儿童是治疗的候选人。在成人中，治疗的治疗目的主要是管理全身性骨痛和增强有限的移动性，如果出现，以及治疗任何非-union骨折。在儿童中，一旦患者达到成人身高和骨骺融合，治疗的目的是纠正或减小型骨软化症，通过放射学异常和骨骼疼痛的缓解来评估。

###临床证据

一项随机、开放标签研究（NCT 02163577）在52名预青春期XLH患者中比较了burosumab，每两周一次。完成16周剂量梯度后，患者接受了burosumab，每2周48次。没有患者在64周的研究中停止了burosumab。患者剂量是个性化以达到目标血清磷浓度3.5到5.0 mg/dL为基础的每天磷水平的治疗。26名患者每两周接受burosumab治疗，直到达到最大剂量2 mg/kg。平均剂量为0.73 mg/kg（范围：0.3, 1.5）在第16周，0.98 mg/kg（范围：0.4, 2.0）在第40周和1.04 mg/kg（范围：0.4, 2.0）在第60周。26名患者中，有8名患者在第40周和第64周接受了burosumab治疗。在研究开始时，患者的平均年龄为8.5岁，46%男性。在治疗中，使用口服磷酸盐和活性维生素D类似物，96%的患者研究期间参与了研究。研究期间收集了这些患者的血清磷和RGI-C得分。在40周后，血清磷从2.5 (0.28) mg/dL基线降至3.5 (0.49) mg/dL。20名患者完成至少48周的研究。

###适用代码

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| E83.31       | 家族性低磷血症

###执业信息

Crysvita®（Burosumab-Twza）（仅限路易斯安那州）

UnitedHealthcare Community Plan医疗福利政策

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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 had used phosphate and/or active vitamin D within 2 years of study baseline. At baseline, all patients had skeletal pain associated with XLH or osteomalacia. The baseline mean (SD) serum phosphorus concentration was below the lower limit of normal at 1.98 (0.31) mg/dL. Oral phosphate and active vitamin D analogs were not allowed during the study with one patient in the burosumab group discontinued treatment. Through week 24, a total of 94% of patients receiving burosumab achieved a serum phosphorus level above the lower limit of normal compared to 8% in the placebo group. Assessment of active fracture/pseudofractures at week 24 demonstrated a higher rate of complete healing in the group receiving burosumab compared to placebo. During the study, a total of 6 new fractures or pseudofractures appeared in 68 patients receiving burosumab, compared to 8 new abnormalities in 66 patients receiving placebo. The FDA conducted its own analysis in order to examine pain medication usage during burosumab treatment. The FDA determined that there is insufficient evidence to support that burosumab decreased use of pain medication during therapy. The FDA stated that it is possible that as longer term data is collected, a significant reduction in pain medication may become evident.\(^1,5\)

A 48-week, open-label, single-arm study (NCT 02537431) was completed in 14 adult XLH patients to determine the effects of burosumab on improvement of osteomalacia as based on histologic and histomorphometric evaluation of iliac crest bone biopsies. Treatment was 1 mg/kg burosumab every four weeks. At study entry, the mean age of patients was 40 years (range 25 to 52 years) and 43% were male. Oral phosphate and active vitamin D analogs 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) declined in 6 patients from a mean (SD) of 594 (675) days to 156 (77) days, a change of -74%.\(^1,5\)

The pharmacokinetics, efficacy, and safety profile of burosumab was evaluated in a Phase 3 randomized, double blind, placebo controlled trial. The primary endpoint was the proportion of subjects achieving mean serum phosphate above 2.5 mg/dL at the dose interval mid-points of the dose interval between baseline and week 24. 94.1% of burosumab-treated subjects vs 7.6% of placebo-treated subjects achieved mean serum phosphorus > the lower limit of normal at mid-point of the dose interval, averaged across dose cycles (P<0.0001). At week 24, treatment was associated with healing of active fractures as well as pseudofractures in 44% of patients in the treatment group compared to 18% in the placebo group. The overall safety profile of patients on burosumab was similar to that of placebo.\(^2\)

**U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

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

**CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)**

Medicare does not have a National Coverage Determination (NCD) for Crysvita\(^\text{®}\) (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](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/761068Orig1s000MultidisciplineR.pdf). (Accessed March 28, 2019)

**REFERENCES**


**POLICY HISTORY/REVISION INFORMATION**

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<td>12/01/2019</td>
<td>Created state-specific policy version for Louisiana (no change to guidelines)</td>
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<tr>
<td>06/01/2019</td>
<td><strong>Template Update</strong>&lt;br&gt;Reorganized policy template:&lt;br&gt;  o Simplified and relocated Application section; previously titled State Exceptions&lt;br&gt;  o Relocated Background and FDA sections</td>
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<td><strong>Supporting Information</strong>&lt;br&gt;Updated CMS section to reflect the most current information; no change to coverage rationale or lists of applicable codes&lt;br&gt;Archived previous policy version CS2019D0071E</td>
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**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.