Reference number(s)
4234-A

STANDARD MEDICARE PART B MANAGEMENT

CRYSVITA (burosumab-twza)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Crysvita is indicated for the treatment of:
1. X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.
2. 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.

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
A. X-linked hypophosphatemia
   1. Initial requests:
      a. Radiographic evidence of rickets or other bone disease attributed to XLH
      b. At least one of the following:
         i. Genetic testing results confirming the member has a PHEX (phosphate regulating gene with homology to endopeptidases located on the X chromosome) mutation
         ii. Genetic testing results confirming a PHEX mutation in a directly related family member with appropriate X-linked inheritance
         iii. Lab test results confirming the member's serum fibroblast growth factor 23 (FGF23) level is above the upper limit of normal or abnormal for the assay
   2. Continuation of therapy requests: documentation (e.g., chart notes, lab test results) of benefit from therapy (e.g., increase or normalization in serum phosphate, improvement in bone and joint pain, reduction in fractures, improvement in skeletal deformities)
B. Tumor induced osteomalacia
   1. Initial requests:
      a. Lab test results confirming the member's serum fibroblast growth factor 23 (FGF23) level is above the upper limit of normal or abnormal for the assay
      b. Fasting serum phosphorus levels less than 2.5 mg/dL

c. Ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) less than 2.5 mg/dL

2. Continuation of therapy requests: documentation (e.g., chart notes, lab test results) of benefit from therapy (e.g., increase or normalization in serum phosphate, improvement in bone and joint pain, reduction in fractures, improvement in skeletal deformities)

III. CRITERIA FOR INITIAL APPROVAL

A. X-linked hypophosphatemia (XLH)

Authorization of 12 months may be granted for treatment of X-linked hypophosphatemia when both of the following criteria is met:

1. The member meets one of the following:
   a. Genetic testing was conducted to confirm a PHEX mutation in the member.
   b. Genetic testing was conducted to confirm a PHEX mutation in a directly related family member with appropriate X-linked inheritance.
   c. Member's FGF23 level is above the upper limit of normal or abnormal for the assay
2. Member has radiographic evidence of rickets or other bone disease attributed to XLH

B. Tumor-induced osteomalacia (TIO)

Authorization of 12 months may be granted for treatment of tumor-induced osteomalacia (TIO) when the following criteria is met:

1. Member's diagnosis is confirmed by ALL of the following:
   a. FGF23 level is above the upper limit of normal or abnormal for the assay
   b. Fasting serum phosphorus levels are less than 2.5 mg/dL
   c. Ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) is less than 2.5 mg/dL
2. Member's disease is associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:

A. The member is currently receiving therapy with the requested medication.
B. The requested medication is being used to treat an indication enumerated in Section III.
C. The member is receiving benefit from therapy (e.g., increase or normalization in serum phosphate, improvement in bone and joint pain, reduction in fractures, improvement in skeletal deformities).

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Crysvita.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex

c. American Hospital Formulary Service- Drug Information (AHFS-DI)
d. Lexi-Drugs
e. Clinical Pharmacology

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Crysvita are covered.

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the diagnostic criteria listed above for X-linked phosphatemia can be found in the design of the confirmational trials. To be eligible for inclusion, the diagnosis of XLH must have been supported by confirmation of phosphate regulating gene with homology to endopeptidases located on the X chromosome (PHEX) mutation in the patient or a directly related family member with appropriate X-linked inheritance, or a serum FGF23 level of greater than 30 pg/mL.

Support for the diagnostic criteria listed above for FGF23-related hypophosphatemia in tumor-induced osteomalacia can be found in the design of the confirmational trials. To be eligible for inclusion, the diagnosis of TIO must have been confirmed by a fasting serum phosphorus level less than 2.5 mg/dL, have an FGF23 level greater than or equal to 100 pg/mL, and have a ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) of less than 2.5 mg/dL.

VII. REFERENCES

1. Crysvita [package insert]. Bedminster, NJ: Kyowa Kirin, Inc.; June 2020.
2. NIH. U.S. National Library of Medicine. ClinicalTrials.gov website. http://clinicaltrials.gov/ct2/show/NCT02163577. Accessed October 24, 2018.
3. NIH. U.S. National Library of Medicine. ClinicalTrials.gov website. http://clinicaltrials.gov/ct2/show/NCT02526160. Accessed October 24, 2018.
4. Dieter, H., Emma, F., Eastwood, D.M., et.al. Clinical Practice Recommendations for the Diagnosis and Management of X-linked Hypophosphataemia. Nature Reviews Nephrology 15, 435-455 (2019).
5. NIH. U.S. National Library of Medicine. ClinicalTrials.gov website. http://clinicaltrials.gov/ct2/show/NCT02304367. Accessed June 30, 2020.
6. Chong WH, Molinolo AA, Chen CC, et.al Tumor-induced Osteomalacia. Endocrine Related Cancer 18:R53-R77 (2011).
7. Fauconnier C, Roy T, Gillerot G, et al. FGF23: Clinical usefulness and analytical evolution. *Clin Biochem.* 2019.