

Crysvita® (burosumab-twza)

When requesting Crysvita® (burosumab-twza) for non-oncology use, the individual requiring treatment must be diagnosed with the following FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Non-Oncology Indication

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

Coverage Guidelines

X-Linked Hypophosphatemia (XLH)

The individual must meet **all** of the following criteria for initial authorization:

- Had a baseline (i.e., prior to any XLH treatment [e.g., Crysvita®, oral phosphate, or vitamin D]) serum phosphorus level that was below the normal range for age;
- Meets one of the following:
 - Had a baseline (i.e., prior to any XLH treatment [e.g., Crysvita®, oral phosphate, or vitamin D]) tubular reabsorption of phosphate corrected for glomerular filtration rate (TmP/GFR) that was below the normal range for age and gender; OR
 - Had a genetic test confirming the diagnosis of X-linked hypophosphatemia via identification of a PHEX pathogenic variant;
- Meets BOTH of the following (*applies to patients 18 years of age and older*):
 - Is currently exhibiting one or more signs or symptoms of X-linked hypophosphatemia (e.g., fractures/pseudofractures, bone and joint pain, muscle weakness, and impaired mobility); AND
 - Has tried oral phosphate and calcitriol therapy unless contraindicated to oral phosphate therapy, calcitriol therapy, or both;
- Crysvita is prescribed by or in consultation with an endocrinologist or nephrologist;

The individual must meet the following criteria for reauthorization:

- Is continuing to benefit from Crysvita (e.g., increased phosphorus levels, radiographic improvement in deformities, healing of fractures/pseudofractures, or reduction in the incidence of new fractures/pseudofractures).

Approval duration (initial and renewal): 12 months

Dosing Recommendations

Adult XLH (18 years of age and older)

The recommended dose regimen is 1 mg/kg body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, administered subcutaneously every 4 weeks.

Pediatric XLH (6 months to less than 18 years of age)

For patients who weigh less than 10 kg, the recommended starting dose is 1 mg/kg of body weight, rounded to the nearest 1 mg, administered subcutaneously every 2 weeks.

For patients who weigh 10 kg and greater, the recommended starting dose regimen is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, administered subcutaneously every 2 weeks. The minimum starting dose is 10 mg up to a maximum dose of 90 mg.

References

1. Crysvita® injection [prescribing information]. Bedminster, NJ/Novato, CA: Kyowa/Ultrogenyx; March 2023.
2. Carpenter TO, Imel EA, Holm IA, et al. A clinician's guide to x-linked hypophosphatemia. *J Bone Miner Res.* 2011;26(7):1381-1388.
3. Haffner D, Francesco E, Eastwood DM, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphatemia. *Nat Rev Nephrol.* 2019;15(7):435-455.
4. Ruppe MD. X-linked hypophosphatemia. GeneReviews®. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK83985/>. Updated April 13, 2017. Accessed on June 26, 2023.
5. Carpenter TO, Whyte MP, Imel EA, et al. Burosumab therapy in children with X-linked hypophosphatemia. *N Engl J Med.* 2018;378(21):1987-1998.
6. Whyte MP, Carpenter TO, Gottesman GS, et al. Efficacy and safety of burosumab in children aged 1-4 years with X-linked hypophosphataemia: a multicenter, open-label, phase 2 trial. *Lancet Diabetes Endocrinol.* 2019;7(3):189-199.
7. Insogna KL, Briot K, Imel EA, et al. A randomized, double-blind, placebo-controlled, phase 3 trial evaluating the efficacy of burosumab, an anti-FGF23 antibody, in adults with X-linked hypophosphatemia: week 24 primary analysis. *J Bone Miner Res.* 2018;33(8):1383-1393.
8. Portale AA, Carpenter TO, Brandi ML, et al. Continued beneficial effects of burosumab in adults with X-linked hypophosphatemia: results from a 24-week treatment continuation period after a 24-week double-blind placebo-controlled period. *Calcif Tissue Int.* 2019;105(3):271-284.
9. Imel EA, Glorieux FH, Whyte MP, et al. Burosumab versus conventional therapy in children with X-linked hypophosphataemia: a randomized, active-controlled, open-label, phase 3 trial. *Lancet.* 2019;393:2416-2427.
10. Briot K, Portale AA, Brandi ML, et al. Burosumab treatment in adults with X-linked hypophosphatemia: 96-week patient-reported outcomes and ambulatory function from a randomized phase 3 trial and open-label extension. *RMD Open.* 2021;7(3):e001714.
11. Linglart A, Imel EA, Whyte MP, et al. Sustained efficacy and safety of burosumab, a monoclonal antibody to FGF23, in children with X-linked hypophosphatemia. *J Clin Endocrinol Metab.* 2022;107(3):813-824.
12. Weber TJ, Imel EA, Carpenter TO, et al. Long-term burosumab administration is safe and effective in adults with X-linked hypophosphatemia. *J Clin Endocrinol Metab.* 2022;108(1):155-165.
13. Kamenicky P, Briot K, Brandi ML, et al. Benefit of burosumab in adults with X-linked hypophosphataemia (XLH) is maintained with long-term treatment. *RMD Open.* 2023;9(1):e002676.