Key Facts about XLH (X-linked hypophosphataemia) and CRYSVITA® (burosumab)

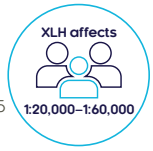
XLH

What is XLH?

XLH is a rare, hereditary, progressive and lifelong renal phosphate wasting disorder caused by mutations in the *PHEX* (phosphate-regulating endopeptidase homolog, X-linked) gene that leads to excess activity of fibroblast growth factor 23 (FGF23)[1–4]

What is the prevalence of XLH?

XLH is a rare disease that affects approximately 1 in 20,000–60,000 people[1,5]



How is XLH inherited?

XLH is inherited in an X-linked dominant pattern; however, 20–30% of cases arise from spontaneous mutations[6,7]

What causes XLH?

XLH is caused by mutations in the PHEX gene,[4,5] which is located on the X chromosome

What does it mean for patients with XLH?

Excess FGF23:

- Decreases renal phosphate reabsorption, which increases urinary phosphate excretion[8]
- Decreases active vitamin D ($1,25[OH]_2D$) production, which reduces intestinal phosphate absorption[8]

The resulting chronic hypophosphataemia impairs bone mineralisation, leading to a variety of clinical manifestations that can impair patients' physical function and quality of life[9]

XLH is **not** just a bone disease – it is a multisystemic disease that impacts muscles and dentition as well[4,10]

CRYSVITA®

What is CRYSVITA®?

- CRYSVITA® is a recombinant, fully human monoclonal antibody IgG1 (immunoglobulin G1) that binds to and inhibits excess FGF23 activity[11]
- It is the first and only disease-modifying biologic treatment that targets the pathophysiology of XLH[12]

How does CRYSVITA® work?

By inhibiting excess FGF23 activity, CRYSVITA® helps restore phosphate homeostasis in people with XLH to improve bone mineralisation, mobility and pain[11–14]

Who can receive CRYSVITA®?

CRYSVITA® is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and paediatric patients 1 year of age and older.[11]

Why use CRYSVITA®?

The efficacy and safety of CRYSVITA® in children aged 1–12 years and adults with XLH have been investigated in a global clinical development programme[12–16]

A phase 3 clinical study in children with XLH showed that compared with continuing conventional therapy, switching children to CRYSVITA®:[13]

- Improved phosphate homeostasis
- Significantly improved rickets healing and reduced its severity up to Week 64
- Significantly improved growth and mobility outcomes up to Week 64
- Significantly improved biochemical markers of phosphate regulation and bone health up to Week 64

In this phase 3 clinical study, CRYSVITA® had an acceptable safety profile over 64 weeks in children with XLH[13]

Phase 3 clinical studies in adults with XLH:

- Phosphate homeostasis, fracture healing, bone mineralisation and remodelling improved, and stiffness were reduced in the CRYSVITA® group compared with the placebo group in a double-blind placebo-controlled study[16]
- Phosphate homeostasis improved, and bone quality, mineralisation and remodelling increased in patients treated with CRYSVITA® by Week 48 when compared with that at baseline in a single-arm study[14]
- There was more healing of baseline fractures/pseudofractures in patients who continued CRYSVITA® compared with those who received CRYSVITA® after placebo at Week 48 in an open-label study[12]
- When placebo-treated patients started CRYSVITA® treatment at Week 24, the healing of fractures/pseudofractures at Week 48 was similar to the healing at Week 24 in those who received CRYSVITA® therapy from the beginning of the study[12]
- CRYSVITA® led to sustained improvements in pain, stiffness and physical function and mobility at Week 48 when compared with that at baseline in a double-blind placebo-controlled study[12]

In these phase 3 studies, CRYSVITA® had an acceptable safety profile up to 48 weeks in adults with XLH[12,14]

REFERENCES **1.** Beck-Nielsen SS, et al. *Eur J Endocrinol.* 2009;160:491–7. **2.** Endo I, et al. *Endocr J.* 2015;62:811–6. **3.** Carpenter TO, et al. *J Bone Miner Res.* 2011;26:1381–8. **4.** Haffner D, et al. *Nat Rev Nephrol.* 2019;15:435–55. **5.** Rafaelsen S, et al. *Eur J Endocrinol.* 2016;174:125–36. **6.** Rajah J, et al. *Eur J Pediatr.* 2011;170:1089–96. **7.** Raimann A, et al. *Wien Med Wochenschr.* 2020;170:116–23. **8.** Razzaque MS. *Nat Rev Endocrinol.* 2009;5:611–9. **9.** Linglart A, et al. *Endocr Connect.* 2014;3:R13–30. **10.** Beck-Nielsen SS, et al. *Orphanet J Rare Dis.* 2019;14:58. **11.** CRYSVITA® (burosumab). Based on Singapore Package Insert. Kyowa Kirin Asia Pacific Pte Ltd; 2021 **12.** Portale AA, et al. *Calcif Tissue Int.* 2019;105:271–84. **13.** Imel EA, et al. Lancet. 2019;393:2416–27. **14.** Insogna KL, et al. *J Bone Miner Res.* 2019;34:2183–91. **15.** Carpenter TO, et al. *N Eng J Med.* 2018;378:1987–98. **16.** Insogna KL, et al. *J Bone Miner Res.* 2018;33:1383–93.

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Kyowa Kirin Hong Kong Co., Limited
Unit B, 13/F., 169 Electric Road, North Point, Hong Kong
Phone : +852 29560828 | Fax : +852 29561627

CRYSVITA®
burosumab

For X-linked hypophosphataemia (XLH)

Abbreviated Package Insert of CRYSVITA® Solution for Injection 10 mg/1mL, 20 mg/1mL, or 30 mg/1mL

Composition:
Burosumab.

Indication:
Treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 yr of age and older.

Dosage & Administration:
Pediatric: BW<10 kg: 1 mg/kg (rounded to the nearest 1 mg), administered q2w. BW>10 kg: starting dose is 0.8 mg/kg (rounded to the nearest 10 mg), administered q2w. The starting dose should between 10 to 90 mg. Dose may be increased to ~2mg/kg (max 90 mg), administered q2w to achieve normal serum P. Adult: 1 mg/kg (rounded to the nearest 10 mg, max dose: 90 mg), administered q4w.

Contraindications:
Concomitant use with oral phosphate &/or active vit D analogs due to the risk of hyperphosphatemia; serum phosphorus is within above the normal range for age; severe renal impairment/ESRD due to abnormal mineral metabolism.

Precautions:
Hypersensitivity; hyperphosphatemia & risk of nephrocalcinosis; injection site reactions; Pregnancy & lactation; Pediatric <1 yr of age; Elderly; Renal impairment.

Common adverse reactions:
For pediatric: pyrexia; injection site reactions, cough, vomiting; pain in extremity; headache; tooth abscess; dental caries.

For adults: back pain; headache; tooth infection; restless leg syndrome; vitamin D decreased; dizziness; constipation; muscle spasms; increase serum P.

Interaction:
Oral phosphate and active vit D analogs.

P/P:
Injection: 10 mg/mL, 20 mg/mL, or 30 mg/mL in a single-dose vial.

Approved version of package insert: Jan 2020

Please refer to the full prescribing information before prescribing. Further information is available upon request.

Kyowa KIRIN
Kyowa Kirin Hong Kong Co., Limited
Unit B, 13/F., 169 Electric Road, North Point, Hong Kong
Phone : +852 29560828 | Fax : +852 29561627