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

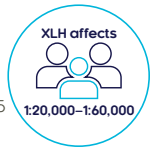
XLH

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; Version 2. Revised FEB 2023 **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.

PLEASE REFER TO THE FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING.
This material is for Healthcare Professionals Only.

Kyowa Kirin Asia Pacific Pte Ltd
80 Robinson Road, #22-01/01A Singapore 068898
Phone : +65 6836 3991 | Fax : +65 6836 3928
E-mail : Info-KKAP@kyowakirin.com

CRYSVITA® burosumab

For X-linked hypophosphataemia (XLH)

CRYSVITA® Abbreviated Product Information

CRYSVITA® (burosumab). Based on Singapore Package Insert. Kyowa Kirin Asia Pacific Pte Ltd; (Date of Revision: FEB 2023)

INDICATIONS AND USAGE

CRYSVITA® is indicated for the treatment of X-linked hypophosphataemia (XLH) in adult and pediatric patients 1 year of age and older.

DOSAGE AND ADMINISTRATION

CRYSVITA is administered by subcutaneous injection and should be administered by a healthcare provider. Discontinue oral phosphate and/or active vitamin D analogs (e.g. calcitriol, paricalcitol, doxercalciferol, calcifediol) 1 week prior to initiation of treatment. Fasting serum phosphorus concentration should be below the reference range for age prior to initiation of treatment. The maximum volume of CRYSVITA per injection is 1.5 mL. If multiple injections are required, administer at different injection sites.

For pediatric patients (1 to less than 18 years of age), the recommended starting dose regimen is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, administered every two weeks. The minimum starting dose is 10 mg up to a maximum dose of 90 mg. After initiation of treatment with CRYSVITA, measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment, and thereafter as appropriate. If serum phosphorus is above the lower limit of the reference range for age and below 5 mg/dL, continue treatment with the same dose. Follow dose adjustment schedule below to maintain serum phosphorus within the reference range for age.

For adult patients (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 every four weeks. After initiation of treatment with CRYSVITA, assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate. If serum phosphorus is within the normal range, continue with the same dose.

CONTRAINDICATIONS

CRYSVITA is contraindicated:

- In concomitant use with oral phosphate and/or active vitamin D analogs (e.g. calcitriol, paricalcitol, doxercalciferol, calcifediol) due to the risk of hyperphosphatemia
- When serum phosphorus is within or above the normal range for age
- In patients with severe renal impairment or end stage renal disease because these conditions are associated with abnormal mineral metabolism.

WARNINGS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions (e.g. rash, urticaria) have been reported in patients with CRYSVITA. Discontinue CRYSVITA if serious hypersensitivity reactions occur and initiate appropriate medical treatment. Hyperphosphatemia and Risk of Nephrocalcinosis: Increases in serum phosphorus to above the upper limit of normal may be associated with an increased risk of nephrocalcinosis. For patients already taking CRYSVITA, dose interruption and/or dose reduction may be required based on a patient's serum phosphorus levels. Injection Site Reactions: Administration of CRYSVITA may result in local injection site reactions. Discontinue CRYSVITA if severe injection site reactions occur and administer appropriate medical treatment.

ADVERSE REACTIONS

The following adverse reactions are described below and elsewhere in the labeling: Hypersensitivity, Hyperphosphatemia and Risk of Nephrocalcinosis and Injection Site Reactions.

Adverse reactions (≥10%) reported in paediatric patients during clinical trials were: Pyrexia, Injection site reaction, Cough, Vomiting, Pain in extremity, Headache, Tooth abscess, Dental caries, Diarrhea, Vitamin D decreased, Constipation, Rash, Nausea, Myalgia, Toothache and Dizziness.

Adverse reactions (>5%) reported in adult patients during clinical trials were: Back pain, Headache, Tooth infection, Restless legs syndrome, Vitamin D decreased, Dizziness, Muscle spasms, Constipation and Blood phosphorus increased.

Please refer to the full prescribing information before prescribing.

Product is approved in selected markets and local approved prescribing information may differ.
Please refer to local approval status and prescribing information.

Kyowa KIRIN

Kyowa Kirin Asia Pacific Pte. Ltd.
80 Robinson Road, #22-01/01A Singapore 068898
Phone : +65 6836 3991 | Fax : +65 6836 3928
E-mail : Info-KKAP@kyowakirin.com