# Key Facts about XLH and CRYSVITA

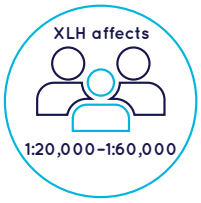
## XLH

### What is XLH?

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

### What is the prevalence?

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




### How is it inherited?

XLH is inherited in an X-linked dominant pattern; however, 20-30% of cases arise from spontaneous mutations[6-8]

### What is XLH caused by?

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
- Decreases active vitamin D (1,25[OH]$_2$D) production, which reduces intestinal phosphate absorption

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) 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[11]

### How does CRYSVITA work?

By inhibiting excess FGF23 activity, CRYSVITA helps restore phosphate homeostasis in children with XLH and improve bone mineralisation[11-12]

### Who can receive CRYSVITA?

CRYSVITA is indicated for the treatment of XLH with radiographic evidence of bone disease in children ≥ 1 years and adolescents with growing skeletons[11]

### Why use CRYSVITA?

The efficacy and safety of CRYSVITA in children aged 1-12 years with XLH have been proven in a global clinical development programme[12-13]

A phase 3 clinical study showed that compared with continuing conventional therapy, switching children with XLH to CRYSVITA:[12]

- Significantly improved rickets healing and reduced severity
- Significantly improved growth and mobility outcomes
- Significantly improved biochemical markers of phosphate regulation and bone health

In this phase 3 clinical study, CRYSVITA had an acceptable safety profile over 64 weeks in children with XLH[12]

**1.** Beck-Nielsen SS, et al. *Eur J Endocrinol.* 2009;160:491–497. **2.** Endo I, et al. *Endocr J.* 2015;62(9):811–816. **3.** Carpenter TO, et al. *J Bone Miner Res.* 2011;26:1381–1388. **4.** Haffner D, et al. *Nat Rev Nephrol.* 2019;15:435–455. **5.** Rafaelsen S, et al. *Eur J Endocrinol.* 2016;174(2):125–136. **6.** Whyte MP, et al. *J Clin Endocrinol Metab.* 1996;81(11):4075–4080. **7.** Rajah J, et al. *Eur J Pediatr.* 2011;170:1089-1096. **8.** Dixon PH, et al. *J Clin Endocrinol Metab.* 1998;83(10):3615–3623. **9.** Linglart A, et al. *Endocr Connect.* 2014;3:R13–R30. **10.** Beck-Nielsen SS, et al. *Orphanet J Rare Dis.* 2019;14(1):58. **11.** CRYSVITA (burosumab). Summary of Product Characteristics. **12.** Imel EA, et al. *Lancet.* 2019;393:2416–2427. **13.** Carpenter TO, et al. *New Eng J Med* 2018;378:1987-1998.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system found under Section 4.8 of the Summary of Product Characteristics.

**This factsheet is developed and funded by Kyowa Kirin International.**
**Prescribing information is available overleaf. CRYSVITA has a conditional marketing authorisation.**
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**Prescribing Information:**

**CRYSVITA▼ (burosumab) 10, 20 & 30 mg solution for injection**

Please refer to the full Summary of Product Characteristics before prescribing.

**Presentation:** Vials containing 10, 20 or 30 mg of burosumab in 1 ml solution. **Indication:** CRYSVITA is indicated for the treatment of X-linked hypophosphataemia with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons. **Dosage and administration:** Crysvita should be given by subcutaneous injection in the arm, abdomen, buttock or thigh. Treatment should be initiated by a physician experienced in the management of patients with metabolic bone diseases. Oral phosphate and active vitamin D analogues (e.g. calcitriol) should be discontinued 1 week prior to initiation of treatment. Vitamin D replacement or supplementation (with inactive forms) may be started or continued as per local guidelines under monitoring of serum calcium and phosphate. At initiation, fasting serum phosphate concentration should be below the reference range for age. The recommended starting dose is 0.8 mg/kg of body weight given every two weeks. Doses should be rounded to the nearest 10 mg. After initiation of treatment, fasting serum phosphate should be measured every 2 weeks for the first month, every 4 weeks for the following 2 months and thereafter as appropriate. Fasting serum phosphate should also be measured 4 weeks after any dose adjustment. If fasting serum phosphate is within the reference range for age, the same dose should be maintained. It is recommended that fasting serum phosphate is targeted in the lower end of the normal reference range for age. The dose may be increased stepwise by 0.4 mg/kg up to a maximum dose of 2.0 mg/kg, up to a maximum dose of 90 mg. Burosumab should not be adjusted more frequently than every 4 weeks. If fasting serum phosphate is above the reference range for age, the next dose should be withheld, and the fasting serum phosphate reassessed within 4 weeks. The patient must have fasting serum phosphate below the reference range for age to restart burosumab at half of the previous dose, rounding the amount as described above. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Concurrent administration with oral phosphate, active vitamin D analogues. Fasting serum phosphate above the normal range for age. Severe renal impairment or end stage renal disease. **Precautions:** Monitoring for signs and symptoms of nephrocalcinosis is recommended at the start of treatment, at 6 and 12 months, and annually thereafter. Monitoring of plasma alkaline phosphatases, calcium, parathyroid hormone and creatinine is recommended every 6 months (every 3 months for children 1- 2 years) or as indicated. Monitoring of urine calcium and phosphate is suggested every 3 months. Periodic measurement of serum parathyroid hormone and postprandial serum phosphate is advised. To decrease risk of ectopic mineralisation, target fasting serum phosphate in the lower end of the normal reference range for age. Administration should be interrupted in any patient experiencing severe injection site reactions and appropriate medical therapy administered. Burosumab must be discontinued if serious hypersensitivity reactions occur and appropriate medical treatment initiated. **Interactions:** Combining with calcimimetics could potentially exacerbate hypocalcaemia. **Adverse reactions:** Injection site reactions (56%), cough (56%), headache (50%), pyrexia (43%), pain in extremity (40%), vomiting (39%), tooth abscess (35%), vitamin D decreased (32%), diarrhoea (25%), rash (24%), nausea (15%), constipation (11%), dental caries (11%) and myalgia (11%). Injection site reactions (e.g. urticaria, erythema, rash, swelling, bruising, pain, pruritus, and haematoma) were generally mild in severity, occurred within 1 day of medicinal product administration, lasted approximately 1 to 3 days, required no treatment, and resolved in almost all instances. Prescribers should consult the summary of product characteristics in relation to other adverse reactions. **Marketing Authorisation number and list price:** 1 x CRYSVITA 10mg; EU/1/17/1262/001, £2,992. 1 x CRYSVITA 20 mg; EU/1/17/1262/002, £5,984. 1 x CRYSVITA 30 mg; EU/1/17/1262/003, £8,976. **Name and address of the Marketing Authorization holder:** Kyowa Kirin Holdings B.V., Bloemlaan 2, 2132NP Hoofddorp, The Netherlands. **Legal classification:** POM.

**Date of Prescribing Information:** December 2019

CRYSVITA has a conditional marketing authorisation

**Adverse Events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.**
**Adverse events should also be reported to Kyowa Kirin Ltd on +44 (0)1896 664000, email medinfo@kyowakirin.com**

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