Kyowa Kirin Australia Pty Ltd

September 03, 2021

New Medicine Approved for the Treatment of X–linked Hypophosphatemia (XLH)[1]

Crysvita® (burosumab) approved by the Australian Therapeutic Goods Administration for the treatment of XLH in Adults, Adolescents and Children 1 year of age or older.[1]

Kyowa Kirin Australia today announced that Crysvita® has been approved by the Therapeutic Goods Administration (TGA) for the treatment of XLH in adults, adolescents and children 1 year of age or older.[1]

"Crysvita® is the first new kind of medicine for the treatment of XLH in more than forty years[2], and the science shows that it actively targets the cause of the disease,"[1,3] said General Manager of Kyowa Kirin Australia, Simon Dawson.

"Whilst the registration of Crysvita® is a major milestone for our company, our focus is now on securing PBS reimbursement so that Australians living with XLH can be guaranteed long-term affordable access to this important medicine," said Mr Dawson.

XLH is a progressive and life-long disease resulting in painful and debilitating abnormalities in the bones, joints, muscles and teeth.[3,4] It is a rare genetic disease[3,4], estimated to affect fewer than 1300 Australians[5-7], however it's the most common form of hereditary rickets.[8,9] It can sometimes appear in individuals with no family history of the disease but is usually passed down from a parent carrying the defective gene.[10] The genetic defect, located on the X-chromosome, causes an excessive loss of phosphate through the urine and poor absorption from the gut, resulting in chronically low levels of phosphate in the blood.[11] Phosphate is a key mineral needed for maintaining the body's energy levels, muscle function,[12] and healthy bones and teeth.[3,13] XLH is not immediately life-threatening but its burden is life-long and progressive, leading to diminished quality of life[14] as well as a reduction in survival relative to controls.[15] While there is no cure for XLH, therapies aimed at helping to restore phosphate to normal levels within the body may help to improve the symptoms of the disease.[10]

Crysvita® is a recombinant human monoclonal IgG1 antibody that binds to and inhibits the biological activity of fibroblast growth factor 23 (FGF23), present in excess in XLH.[1,3] Neutralisation of FGF23 by Crysvita® increases renal reabsorption of phosphate and the serum concentration of 1, 25 dihydroxy-Vitamin D.[1,3]

Kyowa Kirin is a research-based life sciences company. The company leverages leading-edge biotechnologies centred on antibody technologies to discover innovative new medicines that address unmet medical needs. Crysvita® is the second medicine from Kyowa Kirin to be approved for use in Australia.[16]

Level 7, 68 York Street, Sydney, NSW 2000, Australia | Email: enquiry.kkau@kyowakirin.com | ABN: 47 631 934 453

Kyowa Kirin Australia Pty Ltd

▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

MINIMUM PRODUCT INFORMATION CRYSVITA® (burosumab) solution for injection

THERAPEUTIC INDICATION: CRYSVITA® (burosumab) is indicated for the treatment of X-linked hypophosphataemia (XLH) in adults, adolescents and children 1 year of age or older. **DOSE AND ADMINISTRATION:** The recommended starting dose regimen for paediatrics (children 1-11yrs and adolescents 12-17yrs) is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, every 2 weeks, up to a maximum dose of 90 mg. The recommended dose regimen in adults (18yrs and older) is 1 mg/kg of body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, administered every 4 weeks. Treatment should be initiated and monitored by specialist medical practitioners experienced in the management of patients with metabolic bone disease. Fasting serum phosphate concentration should be below the reference range for age prior to initiation of treatment. CRYSVITA® is administered by subcutaneous injection and should be administered by a healthcare provider. The maximum volume of CRYSVITA® per injection site is 1.5 mL. If multiple injections are required, administer at different injection sites. **CONTRAINDICATIONS:** Hypersensitivity to CRYSVITA® or to any of the excipients. Concurrent administration with oral phosphate and / or active vitamin D analogues. Serum phosphate level within or above the normal range for age at initiation of treatment. Severe renal impairment or end stage renal disease. **PRECAUTIONS:** Discontinue oral phosphate and active vitamin D analogues at least 1 week prior to initiating CRYSVITA® treatment. Monitor for signs and symptoms of nephrocalcinosis, hyperphosphatemia, ectopic mineralisation, and serious hypersensitivity reactions. Administration should be interrupted in any patient experiencing severe injection site reactions. Discontinue if serious hypersensitivity reaction occurs. Monitoring for signs and symptoms of nephrocalcinosis due to ectopic mineralisation, e.g. by renal ultrasonography, is recommended at the start of treatment and every 6 months for the first 12 months of treatment, and annually thereafter. Monitoring of urine calcium and phosphate is suggested every 3 months. Monitoring of plasma alkaline phosphatase, calcium, parathyroid hormone (PTH) and creatinine is recommended every 6 months (every 3 months for children 1 - 2 years) or as indicated. **INTERACTIONS:** Concurrent administration of CRYSVITA® with oral phosphate and active vitamin D analogues is contraindicated as it may cause an increased risk of hyperphosphatemia and hypercalcaemia. Caution should be exercised when combining CRYSVITA® with calcimimetic medicinal products. **ADVERSE EFFECTS:** Very common adverse reactions (>10%) reported in paediatric patients (≥1-17yrs) during clinical trials who had received at least 1 dose of CRYSVITA® were: injection site reactions, cough, headache, pyrexia, pain in extremity, vomiting, tooth abscess, vitamin D decreased, diarrhoea, rash, nausea, constipation, dental caries and myalgia. Common adverse reactions (≤10%) reported in paediatric patients ≥1 year of age during clinical trials who had received at least 1 dose of CRYSVITA® were: dizziness and blood phosphorus increased. Very common adverse reactions (>10%) reported in adult patients (≥18yrs) who had received at least 1 dose of CRYSVITA® during clinical trials were: back pain, headache, tooth infection, restless legs syndrome, muscle spasms, vitamin D decrease and dizziness. Common adverse reactions (≤10%) reported in adult patients who had received at least 1 dose of CRYSVITA® during clinical trials were: constipation and blood phosphorus increased. Content based on full CRYSTVITA® Product Information. Date Approved: 03Sept2021.
Please review full Product Information before prescribing. Product Information is available at:
https://www.kyowakirin.com/australia/our_medicines/doc/crysvita_product_information_leaflet.pdf

www.kyowakirin.com/australia. enquiry.kkau@kyowakirin.com. KKAU-XLH-2108062. Date of preparation September 2021.

PBS Information: This medicine is not available through the PBS.

Please review the Consumer Medicines Information here or the full Product Information here for further safety information.

Media enquiries:
Simon Dawson
General Manager
+61 456 550 405

simon.dawson.m4@kyowakirin.com

References:

1. Australian Product Information for CRYSViTA® (burosumab) approved 03 Sep 2021. Available at: https://www.kyowakirin.com/australia/our_medicines/doc/crysvita_product_information_leaflet.pdf. Last accessed September 2021.
2. Collins M. Burosumab: At Long Last, an Effective Treatment for FGF23-Associated Hypophosphatemia. Journal of Bone and Mineral Research, Vol. 33, No. 8, August 2018, pp 1381–1382
3. Padidela R, et al. Clinical guidelines for burosumab in the treatment of XLH in children and adolescents: British paediatric and adolescent bone group recommendations. Endocr Connect. 2020 Oct;9(10):1051-1056.
4. Padidela R, et al. The international X-linked hypophosphataemia (XLH) registry (NCT03193476): rationale for and description of an international, observational study. Orphanet Journal of Rare Diseases 2020 15:172.
5. Beck-Nielsen SS, et al. Incidence and prevalence of nutritional and hereditary rickets in southern Denmark. European Journal of Endocrinology 2009 160 491–497
6. Australian Bureau of Statistics. Population Clock. 2021. Available at: https://www.abs.gov.au/ausstats/abs%40.nsf/94713ad445ff1425ca25682000192af2/1647509ef7e25faaca2568a900154b63?OpenDocument. Accessed 17 February, 2021.
7. Kyowa Kirin. Data on file. 2021
8. Imel EA, et al. Burosumab versus conventional therapy in children with X-linked hypophosphataemia: a randomised, active-controlled, open-label, phase 3 trial. Lancet 2019 Jun 15;393(10189):2416-2427
9. Carpenter TO, et al. A clinician's guide to X-linked hypophosphatemia. J Bone Miner Res. 2011;26:1381-8.
10. Dahir K, et al. X-Linked Hypophosphatemia: A New Era in Management. Journal of the Endocrine Society, 2020, Vol. 4, No. 12, 1–15
11. Beck-Nielsen SS, et al. FGF23 and its role in X-linked hypophosphatemia-related morbidity. Orphanet J Rare Dis. 2019;14:58.
12. Pesta D, et al. Hypophosphatemia promotes lower rates of muscle ATP synthesis. The FAESB Journal. 2016;39:3378-3387
13. Unnanuntana A, et al. Diseases affecting bone quality: beyond osteoporosis. Clin Orthop Relat Res. 2011;469:2194-2206. Skrinar A, et al. The lifelong impact of X-linked hypophosphatemia: Results from a burden of disease survey. J Endocr Soc. 2019;3:1321-1334.
14. Skrinar A, et al. The lifelong impact of X-linked hypophosphatemia: Results from a burden of disease survey. J Endocr Soc. 2019;3:1321-1334.
15. Hawley, S. et al. Prevalence and Mortality of Individuals With X-Linked Hypophosphatemia: A United Kingdom Real-World Data Analysis, Clin Endocrinol Metab, March 2020, 105(3):e871–e878.
16. Therapeutic Good Administration. Australian Register of Therapeutic Goods. 2021. Available at: https://www.tga.gov.au/australian-register-therapeutic-goods. Accessed September 2021

www.kyowakirin.com/australia KKAU-XLH-2109071. Date of preparation September 2021.