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News release

Kyowa Kirin Receives Positive CHMP Opinion for the Self-administration of CRYSVITA® ▼ (burosumab) to Treat X-Linked Hypophosphataemia (XLH), a Rare Metabolic Bone Disorder

Self-administration of CRYSVITA could offer additional options for healthcare professionals to meet the needs of XLH patients and their carers, ensuring continuity of therapy during and beyond the COVID-19 pandemic

TOKYO, Japan, 6 May 2021 – Kyowa Kirin Co., Ltd. (TSE:4151, Kyowa Kirin) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended that CRYSVITA® (burosumab) be approved for the option of self-administration for the treatment of X-linked hypophosphataemia (XLH), a rare metabolic bone disease that impacts children and adults. The Committee indicated that, in addition to healthcare professionals, some patients or carers may be suitable to administer CRYSVITA, at the recommendation of the treating physician in its licensed indication for the treatment of XLH in children and adolescents aged 1 to 17 years with radiographic evidence of bone disease, and in adults.[1]

Abdul Mullick, President of Kyowa Kirin International, said: "The global pandemic has seen huge demands placed on healthcare systems, which has greatly impacted patient care. COVID-19 has also made some patients reluctant to visit healthcare facilities for fear of infection or of interrupting critical care of patients diagnosed with coronavirus. One of the ways in which Kyowa Kirin can help is by giving healthcare professionals increased flexibility to help patients receive treatment in the way that best suits their needs. The self-administration of CRYSVITA is a great example of meeting physician and patient needs and is one of the ways in which we are delivering on our purpose, to make people smile."

CRYSVITA is administered by subcutaneous injection.[1] CRYSVITA treatment will still need to be initiated by a physician experienced in the management of patients with metabolic bone diseases. Subsequently, if the patient is receiving a stable dose, the physician may recommend that administration can be performed by the patient or carer following appropriate training. The first self-administrated dose after drug initiation or dose change will need to be conducted under the supervision of a healthcare professional.

Dr Raja Padidela, Consultant Paediatric Endocrinologist at Royal Manchester Children's Hospital, UK said: "Self-administration of medicines can help some patients maintain their independence and also empower them to take better control of their condition. In addition to XLH patients with mobility issues, this news could also be of benefit to parents of younger children with XLH, who may have less time to attend appointments at health centres or accommodate visits from home care nurses for administering injections. Many injectable treatments

for chronic diseases, such as insulin for the treatment of diabetes mellitus, are successfully self-administered by patients. For XLH patients, the treating physician will assess which patients are appropriate, ensuring those self-administering are competent and comfortable doing so."

The European Commission (EC) will review the CHMP recommendation and a final decision on the variation application to add the option of self-administration of CRYSVITA to the current approved SmPC is expected in the coming months. Self-administration of CRYSVITA remains unlicensed until the EC decision is issued.

▼This medicinal product is subject to additional monitoring.

About X-linked hypophosphataemia

X-linked hypophosphataemia (XLH) is a rare, genetic disease that causes abnormalities in the bones, muscles, and joints.[2,3] XLH is not life-threatening, but its burden is life-long and progressive, and it may reduce a person's quality of life.[4]

People with XLH have a genetic defect on the X-chromosome, which 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.[4,5] Phosphate is a key mineral needed for maintaining the body's energy levels, muscle function, and the formation of healthy bones and teeth.[6,7] 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.[8]

XLH is the most common form of hereditary rickets.[9] It can sometimes appear in individuals with no family history of the disease, but is usually passed down from a parent who carries the defective gene.[10]

About CRYSVITA® (burosumab)

CRYSVITA (burosumab) was created and developed by Kyowa Kirin and is a recombinant fully human monoclonal IgG1 antibody against the phosphaturic hormone fibroblast growth factor 23 (FGF23). FGF23 is a hormone that reduces serum levels of phosphate by regulating phosphate excretion and active vitamin D production by the kidney. Phosphate wasting and resulting hypophosphataemia in X-linked hypophosphataemia (XLH) is caused by excess FGF23. CRYSVITA is designed to bind to, and thereby inhibit, the biological activity of FGF23. By blocking excess FGF23 in patients, CRYSVITA is intended to increase phosphate reabsorption from the kidney and increase the production of active vitamin D, which enhances intestinal absorption of phosphate and calcium.

CRYSVITA has been available for clinical use since 2018. The first approval came from the European Commission, that granted a conditional marketing authorisation for CRYSVITA for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. In 2020, this authorisation was subsequently expanded to include older adolescents and adults.[1]

CRYSVITA is approved by the US Food and Drug Administration (FDA) for patients with XLH aged 6 months and older and by Health Canada for patients with XLH aged one year and older.[11,12]

In 2019, CRYSVITA received approval from Japan's Ministry of Health, Labour and Welfare for the treatment of FGF23-related hypophosphataemic rickets and osteomalacia. In 2020, CRYSVITA was reimbursed by National Health Insurance (NHI) in Japan as a self-injection presentation for the treatment of FGF23-related hypophosphataemic rickets and osteomalacia.

In January 2020, Swissmedic approved CRYSVITA for the treatment of adults, adolescents and children (one year of age and older) with XLH.[13]

Kyowa Kirin and Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE: Ultragenyx) have been collaborating in the development and commercialisation of CRYSVITA globally, based on the collaboration and licence agreement between Kyowa Kirin and Ultragenyx.

About Kyowa Kirin

Kyowa Kirin strives to create and deliver novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company with a heritage of 70+ -years, we apply cutting-edge science including an expertise in antibody research and engineering, to address the needs of patients and society across multiple therapeutic areas including Nephrology, Oncology, Immunology/Allergy and Neurology. Across our four regions – Japan, Asia Pacific, North America and EMEA/International – we focus on our purpose, to make people smile, and are united by our shared values of commitment to life, teamwork/Wa, innovation, and integrity. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com/

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