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30th September 2025

Crysvita (burosumab): Risk of severe hypercalcaemia

Dear Healthcare Professional,

Kyowa Kirin in agreement with the European Medicines Agency and the Malta Medicines Authority would like to inform you of important safety information regarding the use of burosumab:

Summary

- **Increases in serum calcium, including severe hypercalcaemia, and/or parathyroid hormone have been reported in patients treated with burosumab.**
- **In particular, severe hypercalcaemia has been reported in subjects with tertiary hyperparathyroidism.**
- **In patients with moderate to severe hypercalcaemia (> 3.0 mmol/L), burosumab should not be administered until hypercalcaemia is adequately treated and resolved.**
- **Monitoring for patients treated with burosumab should include:**
    - **serum calcium before initiation of treatment, 1-2 weeks after initiation and dose adjustments, and during treatment every 6 months (every 3 months for children aged 1-2 years),**
    - **parathyroid hormone every 6 months (every 3 months for children aged 1-2 years).**
- **Factors such as hyperparathyroidism, prolonged immobilisation, dehydration, hypervitaminosis D or renal impairment may increase the risk of hypercalcaemia.**

Background on the safety concern

Crysvita (burosumab) is indicated for the treatment of:

- X-linked hypophosphataemia (XLH), in children and adolescents aged 1 to 17 years with radiographic evidence of bone disease, and in adults.
- FGF23-related hypophosphataemia in tumour-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumours that cannot be curatively resected or localised in children and adolescents aged 1 to 17 years and in adults.

Cases of severe hypercalcaemia have been reported in the post-marketing setting in patients treated with burosumab who have tertiary hyperparathyroidism associated with other risk factors for hypercalcaemia.

Initiation of burosumab may affect calcium levels due to restoration of phosphate homeostasis. The effect on parathyroid hormone as a result of burosumab inhibition of FGF23 is, however, unknown.

To prevent occurrence of severe hypercalcaemia in vulnerable patients, the following is recommended:

- Serum calcium and parathyroid hormone levels should be monitored before and during burosumab treatment. Serum calcium should be measured 1-2 weeks after burosumab initiation and in case of dose adjustment. Calcium and parathyroid hormone should be determined every 6 months (every 3 months for children aged 1-2 years).
- Particular attention should be given to patients with underlying tertiary hyperparathyroidism since they are at risk of developing moderate to severe hypercalcaemia. Other risk factors

for hypercalcaemia, such as prolonged immobilisation, dehydration, hypervitaminosis D, or renal impairment, must also be considered and adequately managed.

- Hypercalcaemia should be controlled, following local clinical practice guidelines, before burosumab initiation or if identified during treatment.

The product information is being revised to include this new information. Hyperparathyroidism, hypercalcaemia, hypercalciuria, and blood parathyroid hormone increased are being added as possible adverse reactions for burosumab, and recommendations for monitoring are being incorporated.

Call for reporting

As a reminder, reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Section 4.8 of the SmPC and Section 4 of the package leaflet . Please ensure to report the product strength and batch details as well.

In accordance with the national requirements, suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form, which is available online at http://www.medicinesauthority.gov.mt/adrportal, and sent by post or email to;

P: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000

E: postlicensing.medicinesauthority@gov.mt including batch/Lot number if available.

Alternatively, any ADRs can be reported to AM Mangion Ltd. Mangion Building, New Street off Valletta Road Luqa LQA 6000 Tel +356 23976333 or e-mail: pv@ammangion.com.

Company contact point

For further enquiries concerning this information, please contact Genesis Pharma Cyprus Ltd, CONSULCO BUILDING, 73 Metochiou Str, 2nd & 3rd Floor, 2407 Engomi, P.O. Box 23638, 1684 Nicosia tel.:+357 22765715, info-cyprus@genesispharmagroup.com.