Erivedge (vismodegib): Risk of premature epiphyseal fusion

Roche Hong Kong Limited (Roche HK), a registration certificate holder of pharmaceutical product, informed the Department of Health (DH) that cases of premature fusion of the epiphyses (growth plates) have been reported in pediatric patients with the use of Erivedge (vismodegib).

Roche HK reminded healthcare professionals of the following:

- Postnatal developmental defects including premature closure of the epiphyseal plate were observed in vismodegib treated rats.
- Erivedge is approved for use in adult patients with advanced basal cell carcinoma where surgery is inappropriate.
- Erivedge is not approved for pediatric use.
- Erivedge could cause epiphyseal closure prior to skeletal maturity.

Three cases of premature epiphyseal fusion in pediatric patients have recently been reported with Erivedge treatment, two of which were within the setting of a clinical trial and one case was from off-label use. All cases were medulloblastoma patients whose ages were approximately 2, 5, and 7 years old at the time of Erivedge initiation. All patients completed radiation and chemotherapy prior to treatment with Erivedge. At the time when epiphyseal closure was diagnosed, the 2-year-old patient, who had recurrent disease, was treated with 4 months of Erivedge, while the older two patients completed 12 months of Erivedge as maintenance treatment in a clinical trial. In 2 of 3 cases, the fusion of the growth plate appeared to progress even after treatment discontinuation.

These findings confirm the risk that was identified based on observation of irreversible closure of the femoral epiphyseal growth plate in a 26-week chronic toxicity and toxicokinetic study in rats at doses ≥ 50 mg/kg/day (corresponding to 0.4 times the steady-state AUC$_{0-24h}$ observed in patients).

Roche advised healthcare providers or investigators to inform patients, as well as a patient’s guardian (as applicable), who have not reached skeletal maturity, of this risk. Roche is working closely with health authorities to update the product label to reflect the risk of premature epiphyseal fusion in patients.

In Hong Kong, Erivedge Capsules 150mg (HK-63786) is a pharmaceutical product registered by Roche HK, and is a prescription only medicine. Roche HK notified DH
that the company is going to issue a “Dear Healthcare Professional Letter” on the
above risk. So far, DH has not received any adverse drug reaction case related to the
product. Roche HK is going to submit application to update the package insert of the
product to include the relevant information. DH will remain vigilant on any safety
update from overseas drug regulatory authorities.

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