GlaxoSmithKline (MALTA) Limited
1 (1st floor) | De la Cruz Avenue | Qormi
QRM 2458 | Malta

Tel: (+356) 21238131
Fax: (+356) 21225417
www.gsk.com

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Restrictions for use of Trobalt® (retigabine) - treatment may lead to pigment changes of ocular tissues, including retina, and skin, lips and/or nails

Dear Healthcare Professional

GlaxoSmithKline (GSK) would like to inform you of a restriction of the indication for Trobalt® (retigabine) following reports of pigment changes and provide you with recommendations for monitoring.

Summary

- Trobalt® should now only be used as adjunctive treatment of drug-resistant partial onset seizures with or without secondary generalisation in patients aged 18 years or older with epilepsy, where other appropriate drug combinations have proved inadequate or have not been tolerated.
- Pigment changes (discolouration) of ocular tissue, including the retina, have been reported in long-term clinical studies with retigabine.
- Blue-grey discolouration of the nails, lips and/or skin have also been observed in these studies.
- Patients currently receiving treatment should be reviewed at a routine (non-urgent) appointment. The balance of benefits and risks should be re-evaluated, and patients should be informed of the risk of pigmentation with long term treatment.
- A comprehensive ophthalmological examination (including visual acuity test, slit-lamp examination, and dilated fundoscopy) should be performed at treatment start and at least every 6 months thereafter while treatment is ongoing. Patients already treated with retigabine should have an appointment scheduled for an ophthalmological examination.
- If retinal pigment or vision changes are detected, treatment with Trobalt should only be continued after a careful re-assessment of the balance of benefits and risks. Also in patients who develop discolouration of the nails, lips or skin, treatment with Trobalt should only be continued after a careful re-assessment of the balance of benefits and risks.

Further information on the safety concern

Trobalt® (retigabine) is now indicated as adjunctive treatment of drug-resistant partial onset seizures with or without secondary generalisation in patients aged 18 years or older with epilepsy, where other appropriate drug combinations have proved inadequate or have not been tolerated.

Among the patients treated with retigabine in two long-term clinical studies and the associated compassionate use programme, eye examinations in 55 patients were completed up to 2 May 2013. Baseline eye assessments were not performed in these studies. Twenty-one cases of pigment changes (discolouration) of ocular tissue, including 15 involving the retina have been reported. Five patients had worse than 20/20 visual acuity. One of these patients had visual acuity of 20/160 in one eye, while the remaining four had visual acuity of 20/25 to 20/40 in one or both eyes.

Mild abnormalities on retinal electrophysiology tests have been reported in two further subjects, both of whom had visual acuity reported to be normal. In one of those subjects, a generalised reduction in the visual fields of both eyes on Humphrey Visual Testing was also noted.

Up to 2 May 2013, 51 cases with events relating to discolouration/ pigmentation of the nails, lips and/or skin after treatment with retigabine were received from the two long-term clinical studies and the compassionate use programme. The events generally presented after long-term exposure to retigabine, with a median time to onset of 4.4 years (range 4 months to 6.7 years) (time to onset refers to date discolouration events were first reported; in some cases the patient is described as having the event(s) before mentioning them to the investigator). There appeared to be no relation with age or gender. Events tended to occur at higher doses, usually 900 mg/day or higher.

The changes described above have been observed in a high proportion of patients who were still ongoing in the long-term studies. About one third of the patients examined so far have presented with retinal pigment changes. The cause, natural history and long-term prognosis of the changes are currently unknown, and further investigative work is ongoing.

Reports of pigmentation/discolouration are considered to be very common adverse events (≥1/10) following prolonged treatment with retigabine.

The Summary of Product Characteristics and Package Leaflet are being revised to include information on the amended indication and these safety risks.

Call for reporting

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

Healthcare professionals should continue to report any adverse events suspected to be associated with the use of Trobalt® to GSK: by post to GlaxoSmithKline (Malta) Limited, 1, 1st floor, de la Cruz Avenue, Qormi, QRM 2458; by phone to 21238131; or e-mail at mt.info@gsk.com, as appropriate.

Any suspected adverse reaction and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Communication Information

Should you have any questions or require additional information please contact GlaxoSmithKline (Malta) Limited, 1, 1st floor, de la Cruz Avenue, Qormi QRM 2458, Malta (Tel. 21 238131). The information contained in this letter has been endorsed by the European Medicines Agency and national Competent Authorities.

Yours sincerely

Ruth M. Gatt
Medical & Regulatory Affairs Executive
GlaxoSmithKline (MALTA) Limited
✉: ruth.m.gatt@gsk.com
☎: (+356) 25675 113