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27th September 2012

Direct Healthcare Professional Communication on restriction of indications for Trimetazidine containing products.

Dear healthcare professional,

Summary

- Trimetazidine-containing products should only be prescribed in adult patients as add-on therapy for the symptomatic treatment of stable angina pectoris inadequately controlled by first-line anti-anginal therapies or to patients intolerant to such therapy.
- The benefit/risk profile of Trimetazidine is no longer indicated in the symptomatic treatment of vertigo and tinnitus and the symptomatic treatment of the decline in visual acuity and visual field disturbances presumably of vascular origin. Patients currently on treatment should have their treatment reviewed at the next routine appointment.
- Trimetazidine should not be used in patients with Parkinson disease, parkinsonian symptoms, tremors, restless leg syndrome, and other related movement disorders.
- Trimetazidine should not be used in patients with severe renal impairment. For patients with moderate renal impairment and the elderly the dose should be reduced.

Further information

Following a review of all available data, the CHMP (The European Medicines Agency´s committee for Medicinal Products for Human Use) concluded that the benefit/risk balance of Trimetazidine-containing products only remains positive in a limited population of patients with stable angina pectoris who are inadequately controlled by or intolerant to first-line anti-anginal therapies as add-on therapy. For all other indications, the efficacy has not been considered as sufficiently documented according to current guidelines and methodology. Thus, the Committee found that the risk outweighed the evidence for clinically important efficacy and concluded that all other indications should be withdrawn from the marketing authorisations of these medicines.

The safety review focused on the occurrence of parkinsonian symptoms which can be associated with the use of trimetazidine. Trimetazidine can cause or worsen parkinsonian symptoms (tremor, akinesia, hypertonia), which should be investigated, especially in elderly patients and patients with renal insufficiency in whom an increased exposure is expected.

Therefore, trimetazidine is contraindicated in patients with Parkinson disease, parkinsonian symptoms, tremors, restless leg syndrome and other movement and in patients with severe renal impairment.

The occurrence of movement disorders such as parkinsonian symptoms, restless leg syndrome, tremors, gait instability should lead to definitive withdrawal of trimetazidine. Cases which have been reported are usually reversible after treatment discontinuation. For the majority of the patients who recovered, the

symptoms disappeared within 4 months after trimetazidine withdrawal. If parkinsonian symptoms persist more than 4 months after drug discontinuation, a neurologist opinion should be sought. Overall, in doubtful cases, patients should be referred to a neurologist for appropriate investigations.

For further information, please refer to the attached Summary of the Product Characteristics.

Call for reporting

You are reminded to report any suspected adverse reactions in accordance with the national spontaneous reporting system *to www.imb.ie.*

Communication information

Should you have any questions or require additional information please contact Aoife McAuliffe, Medical and Regulatory Affairs Manager, Servier Laboratories Ireland, Tel: 01-6638110.

Yours sincerely,

Mr Yann Mazeman, PharmD

General Manager