European Medicines Agency recommends the suspension of nicotinic acid/laropiprant medicinal products - Tredaptive, Pelzont and Trevaclyn

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Information on Medicinal Product

Nicotinic acid/laropiprant (authorised under brand names Tredaptive, Trevaclyn and Pelzont) is used for the treatment of adults with dyslipidaemia (abnormally high levels of fat in the blood), particularly 'combined mixed dyslipidaemia' and 'primary hypercholesterolaemia (high levels of cholesterol in the blood), in combination with statins (standard medicines used to lower cholesterol) when the cholesterol lowering effect of statins alone are inadequate or when patients are allergic to statin therapy.

The product is authorised and marketed in Malta as Tredaptive in modified release tablets containing 1000mg of nicotinic acid and 20mg of laropiprant.

Information from European Medicines Agency (EMA) about the safety concern

At the time of authorisation, the marketing authorization holder (MAH) had agreed to conduct a clinical study as part of the activities to monitor this product once it was placed on the market. This study was conducted by the University of Oxford and funded by the MAH and was called the HPS2-THRIVE[1] study. This study was a large, long-term study comparing the clinical effects of adding Tredaptive to statins (standard medicines used to reduce cholesterol) with statin treatment alone.

Initial results of this study became available for review at the end of December 2012 and were presented to the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) in January

[1] HPS2-THRIVE: Hearth Protection Study 2 – Treatment of HDL (high density lipoprotein) to Reduce the Incidence of Vascular Events.

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2013. The PRAC considered all the available evidence provided by the MAH in writing and during an oral explanation.

The results from this study raised questions about the efficacy of the medicine when added to statins, as this did not reduce the risk of major vascular events (serious problems with the heart and blood vessels, including heart attack and stroke) compared with statin therapy alone. In addition, in the preliminary results a higher frequency of non-fatal but serious side effects was seen in patients taking the medicine than in patients only taking statins.

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded that the benefit-risk balance for Tredaptive is negative and has given its recommendation to the Committee on Medicinal Products for Human Use (CHMP). The CHMP is of the opinion that the marketing authorisation of nicotinic acid/laropiprant containing medicinal products including Tredaptive should be suspended and that any available medicinal product should be recalled.

This opinion has been forwarded to the European Commission and a decision will be issued in due course.

Additional information for Healthcare Professionals

- The HPS2-THRIVE study was a large, long-term study involving 25,673 patients considered to be at high risk for cardiovascular events due to a history of occlusive vascular disease. Of those enrolled, 14,741 were from Europe and 10,932 were from China. Patients were followed for a median of 3.9 years.
- The study was designed to assess the effect of adding nicotinic acid / laropiprant to statins on a composite endpoint of major vascular events, which included the combination of coronary death, non-fatal heart attack, stroke and revascularisation. Patients were treated with simvastatin 40 mg or simvastatin 40 mg plus ezetimibe 10 mg to achieve a total cholesterol level of less than 3.5 mmol/l, and were then randomised to nicotinic acid / laropiprant or placebo.
- Treatment with nicotinic acid / laropiprant together with a statin resulted in a non-significant reduction in major vascular events such as heart attack and stroke compared with statin therapy alone.

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- A statistically significant increase in the incidence of non-fatal but serious adverse events was seen. These included bleeding (intracranial and gastro-intestinal), myopathy, infections and new-onset diabetes.
- As taking Tredaptive, Pelzont and Trevaclyn together with a statin has no significant additional benefit in reducing the risk of major vascular events compared with statin therapy alone and taking into account the increased risk of serious side effects, the CHMP recommended the suspension of these medicines.

In Malta

For Healthcare Professionals

- In light of the unfavourable benefit-risk balance of Tredaptive doctors should no longer prescribe this to their patients.
- Doctors should review their patients' treatment in order to discontinue treatment with these medicines, which will no longer be available from the week starting on 21 January 2013.
- Other alternative therapies should be considered in order to manage dyslipidaemia.
- Pharmacists should refer patients on new or repeated prescriptions for Tredaptive, to the treating doctor.

Advice for Patients

- Tredaptive will no longer be available from the week starting on 21 January 2013 as the European Medicines Agency (EMA) has recommended their suspension. This follows the review of new evidence which indicated that the benefits of these medicines no longer outweigh their risks for patients.
- If you are taking Tredaptive you should make an appointment with your doctor to review your treatment.
- Do not stop Tredaptive before speaking to your doctor.

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Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on all medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority yellow card scheme or online at **http://www.medicinesauthority.gov.mt/pub/adr.doc** or to the marketing authorisation holder or their local representatives.>

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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