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Tredaptive, Pelzont and Trevaclyn suspended across the EU

Doctors should no longer prescribe these medicines and should review patients' treatment options

On 17 January 2013, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) confirmed the recommendation to suspend the marketing authorisations of Tredaptive, Pelzont and Trevaclyn (nicotinic acid / laropiprant) used to treat adults with dyslipidaemia (abnormally high blood levels of fats such as triglycerides and cholesterol). The CHMP opinion was based on a recommendation by the Pharmacovigilance Risk Assessment Committee (PRAC) to suspend these medicines.

The CHMP encouraged patients currently taking these medicines to make a non-urgent appointment with their doctor to discuss their treatment. Doctors should no longer prescribe Tredaptive, Pelzont or Trevaclyn and should review patients' treatment options.

The review of Tredaptive, Pelzont and Trevaclyn was initiated in December 2012 after new data from a large, long-term study called HPS2-THRIVE became available. The results of the study, which are still preliminary, indicated that taking nicotinic acid / laropiprant together with a statin has no significant additional benefit in reducing the risk of major vascular events such as heart attack and stroke, compared with statin therapy alone. In addition, a higher frequency of non-fatal but serious side effects was seen in patients taking these medicines.

Having reviewed the results of the study, the CHMP concluded that the benefits of Tredaptive, Pelzont and Trevaclyn no longer outweigh the risks and that their marketing authorisations should be suspended.

More information on the HPS2-THRIVE study is available below.

The CHMP opinion was sent to the European Commission, which endorsed it and issued a final legally binding decision on 22 March 2013.

Information to patients

- Tredaptive, Pelzont and Trevaclyn are identical medicines used to treat adults with dyslipidaemia (abnormally high blood levels of fats such as triglycerides and cholesterol). Such treatment is

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ultimately aimed to reduce the risk of heart attacks, strokes and other conditions affecting the heart and blood vessels.

- The Agency recommended the suspension of Tredaptive, Pelzont or Trevaclyn following 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, Pelzont or Trevaclyn you will have to discontinue treatment, as these medicines are no longer available in the EU.
- You should make a non-urgent appointment with your doctor to review your treatment.
- If you have any questions, you should contact your doctor or pharmacist.

Information to healthcare professionals

Healthcare professionals should follow these recommendations:

- In light of the unfavourable benefit-risk balance of Tredaptive, Pelzont and Trevaclyn, doctors should no longer prescribe these medicines to their patients.
- Doctors should review their patients' treatment in order to discontinue treatment with these medicines, which are no longer available in the EU.
- Pharmacists should refer patients on new or repeated prescriptions for Tredaptive, Pelzont and Trevaclyn to the treating doctor.

The Agency's recommendations are based on the new data from the HPS2-THRIVE study:

- 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 did not result in a statistically significant reduction in major vascular events such as heart attack and stroke compared with statin therapy alone.
- An 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 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.

More about the medicine

- Tredaptive, Pelzont and Trevaclyn contain two active substances: nicotinic acid (1,000 mg) and laropiprant (20 mg). They were available as modified release tablets (meaning that the two active substances are released at different rates over a few hours).

- Tredaptive, Pelzont and Trevaclyn are identical medicines authorised throughout the EU on 3 July 2008 for the treatment of dyslipidaemia in combination with a statin when statin treatment alone is not sufficient, or alone in patients unable to take statins. The medicine has been marketed under one of these trade names by Merck Sharp & Dohme Ltd in all EU Member States, except Bulgaria, France and Romania.
- The two active substances, nicotinic acid and laropiprant, have different functions. Nicotinic acid is a naturally occurring substance used in low doses as a vitamin (known as niacin or vitamin B3). In higher doses, it reduces the levels of fat in the blood via a mechanism that is not fully understood. It was first used as a medicine to modify blood fat levels in the mid-1950s, but its use has been limited because of its side effects, particularly flushing (reddening of the skin). Laropiprant has no effect on cholesterol but it reduces flushing, by blocking the receptors for a substance called 'prostaglandin D2' which is released when nicotinic acid is taken and which dilates (widens) the blood vessels in the skin.

More about the procedure

- The review of Tredaptive, Pelzont and Trevaclyn was initiated at the request of the European Commission on 19 December 2012, under Article 20 of Regulation (EC) No 726/2004 following the procedural steps laid out in Article 107j and 107k of Directive 2001/83/EC. The European Commission asked the Agency to assess the impact of the new data from the HPS2-THRIVE study, and to issue an opinion on whether the marketing authorisation for these medicines should be maintained, varied, suspended or withdrawn across the EU.
- A review of these data was first conducted by the Pharmacovigilance Risk Assessment Committee (PRAC). The PRAC recommendations were sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for all questions concerning medicines for human use, which adopted the Agency's final opinion. Further information on the PRAC recommendation and the background to this review can be found on Agency's website.
- The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision on 22 March 2013.

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