



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 January 2013
EMA/5817/2013

PRAC considers that benefit-risk balance of Tredaptive, Pelzont and Trevaclyn (nicotinic acid/laropiprant) is negative

Recommendation by PRAC to be considered by CHMP for final opinion

During its January 2013 meeting, the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) concluded that the risks are greater than the benefits for Tredaptive, Pelzont and Trevaclyn, identical medicines used to treat adults with dyslipidaemia (abnormally high blood levels of fats such as triglycerides and cholesterol), and it recommended that these medicines should be suspended.

The PRAC recommendation will be considered by the Agency's Committee for Medicinal Products for Human Use (CHMP), which will adopt a final scientific opinion. The final opinion is expected at the next CHMP meeting of 14-17 January 2013.

Why are Tredaptive, Pelzont and Trevaclyn being reviewed?

The EMA started the review of Tredaptive, Pelzont and Trevaclyn in December 2012 after new data from a large, long-term study involving over 25,000 patients became available, which cast doubt on their benefits. The results of the study, which are still preliminary, indicated that adding these medicines to statins (the standard medicine used to reduce cholesterol) did not reduce 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 the medicines with statins than in patients only taking statins.

Tredaptive, Pelzont and Trevaclyn were authorised in the EU to be given in combination with a statin when statin treatment alone was not sufficient, and could be used alone only in patients unable to take statins.

What are the PRAC conclusions?

The PRAC concluded that the preliminary results of the study clearly showed that taking Tredaptive, Pelzont or Trevaclyn together with a statin has no significant additional benefit in reducing the risk of major vascular events such as heart attack and stroke in patients at high risk of cardiovascular disease (problems with the heart and blood vessels). Although Tredaptive, Pelzont or Trevaclyn effectively reduced levels of triglyceride fat and increase HDL 'good' cholesterol levels, the data from the study did



not show that this led to improved clinical outcomes in patients, and the company has not been able to identify a specific group of patients that could be shown to benefit from the medicines. In addition, the study showed an increased frequency of serious side effects in patients taking these medicines, such as bleeding, muscle weakness, infections and diabetes.

Therefore, in the light of the latest study data, the PRAC considered that the benefit-risk balance for Tredaptive, Pelzont or Trevaclyn is negative, and recommended that the marketing authorisations of these medicines should be suspended.

What will happen next?

The PRAC recommendation will be considered by the CHMP at its meeting of 14-17 January 2013. The CHMP will adopt the Agency's final opinion on whether the marketing authorisations for Tredaptive, Pelzont and Trevaclyn should be maintained, changed, suspended or withdrawn across the EU. The CHMP opinion will be forwarded to the European Commission for the adoption of a legally binding decision.

Further to the EMA's previous communication published on 21 December 2012¹, the final CHMP opinion, together with full advice for patients and healthcare professionals, will be made public. Healthcare professionals in the EU will receive a letter with detailed information on the appropriate actions to be taken.

More about the medicine

Tredaptive, Pelzont and Trevaclyn contain two active substances: nicotinic acid (1000 mg) and laropiprant (20 mg). They are available as modified release tablets (meaning that the two active substances are released at different rates over a few hours).

Tredaptive, Pelzont and Trevaclyn were authorised throughout the EU on 3 July 2008. 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. It follows the procedural steps laid out in Article 107i of Directive 2001/83/EC.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. The PRAC recommendations will now be forwarded to the Committee for

¹ See:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/12/news_detail_001686.jsp&mid=WC0b01ac058004d5c1

Medicinal Products for Human Use (CHMP), responsible for all questions concerning medicines for human use, which will adopt a final opinion. An opinion is expected to be adopted at the CHMP meeting on 14-17 January 2013.