Initiation of the procedure laid down in Article 20 of Regulation (EC) No 726/2004

This is an official initiation by the European Commission of a procedure under Article 20 of Regulation (EC) No 726/2004

Common name:	laropiprant and extended release nicotinic acid
Product name:	Tredaptive, Pelzont and Trevaclyn

Tredaptive, Pelzont and Trevaclyn are fixed dose combination products containing laropiprant and extended release nicotinic acid. The products are indicated for the treatment of dyslipidemia, particularly in patients with combined mixed dyslipidemia and in patients with primary hypercholesterolemia.

The products are available as modified release tablets containing 20 mg of laropiprant and 1000 mg of nicotinic acid and were approved in the European Union on 3 July 2008.

The MAH has been conducting a randomized clinical outcome study of the long-term clinical effects of raising HDL cholesterol with laropiprant/extended release nicotinic acid called HPS2-THRIVE study (Heart Protection Study 2-Treatment of HDL to Reduce the Incidence of Vascular Events), to assess the incremental benefit of laropiprant/extended release nicotinic acid versus placebo on top of simvastatin 40 mg, with or without ezetimibe, in 25,000 high-risk patients in the UK, Scandinavia, and China. The follow-up of this study was part of the risk management plan agreed by the CHMP at the time of the authorisation and therefore part of the pharmacovigilance activities of the marketing authorisation holder.

On 17 December 2012, the MAH informed the EMA of the preliminary results from HPS2-THRIVE, which show that the study did not meet its primary endpoint of reduction of major vascular events. Adding laropiprant/extended release nicotinic acid to statin therapy did not further reduce the risk of the combination of coronary deaths, non-fatal heart attacks, strokes or revascularizations compared to statin therapy.

In addition, there was a statistically significant increase in the incidence of non-fatal serious adverse events in the laropiprant/extended release nicotinic acid group compared to the statin group. These imbalances occurred in several System Organ Classes (SOC), some of which reflect anticipated risks based on the known profile of nicotinic acid or earlier safety analyses of this trial (e.g. myopathy, new onset diabetes) and others which were unanticipated (e.g. infections).

In light of the current emerging data resulting from pharmacovigilance activities, which may suggest new risks or changed risks, there is a need to review all data on this fixed combination and their impact on the benefit-risk of Tredaptive, Pelzont and Trevaclyn.

Therefore, the European Commission (EC) initiates a procedure under Article 20 of Regulation (EC) No 726/2004 and requests the opinion of the Agency within the time-limits provided by Article 107j and 107k of Directive 2001/83/EC. The EC requests the Agency to assess the above safety concerns and their impact on the benefit/risk balance of the centrally authorised medicinal products Tredaptive, Pelzont and Trevaclyn and to give its opinion on whether the marketing authorisations for these products should be maintained, varied, suspended or withdrawn. As the request results from the evaluation of data resulting from pharmacovigilance activities the opinion of the Agency should be adopted by the Committee for Medicinal Products for Human Use on the basis of a recommendation of the Pharmacovigilance Risk Assessment Committee.

Having regard to the potential serious consequences for public health, the CHMP is asked to consider, if there is a need to take provisional measures, notably a suspension of use of the medicinal products.

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