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PRAC recommends using acipimox only as additional or alternative treatment to lower high triglyceride levels

Licensed uses should be refined to optimise benefit-risk

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended that medicines containing acipimox should have their marketing authorisations amended to ensure that they are used across the European Union only as an additional or alternative treatment in type IIb and type IV hyperlipoproteinaemia. These are conditions involving hypertriglyceridaemia (high levels of triglycerides, a type of fat, in the blood), with or without increased cholesterol. Acipimox-containing medicines should be used when changes in lifestyle, including diet and exercise, and treatment with other medicines are not adequate. The available evidence does not support wider use in lipid disorders (abnormal levels of fats in the blood).

The original reason for the review of acipimox was HPS2-THRIVE, a large study which looked at the long-term effect of the combination of nicotinic acid (a substance related to acipimox) and another medicine, laropiprant, in treating lipid disorders. The study showed that this combination taken together with statins (another class of medicines used to treat lipid disorders) did not lead to additional benefits in reducing the risk of major vascular events such as heart attack and stroke, but did result in a higher frequency of non-fatal but serious side effects. As a result, the European Medicines Agency recommended the suspension of medicines containing the combination of nicotinic acid and laropiprant across the EU.[1] Because acipimox was the only other medicine containing nicotinic acid or a related substance that was currently marketed for lipid disorders in the EU, its benefit-risk balance was reviewed in the light of the latest evidence.

The PRAC considered available data from the HPS2-THRIVE study and from studies with acipimox and evidence from the literature, as well as spontaneous reports of adverse effects and advice from a group of experts in the treatment of lipid disorders.

The results from the HPS2-THRIVE study could not be directly extrapolated to acipimox, since the study included combination with another medicine, laropiprant, whose effects were not established. Possible differences between nicotinic acid and acipimox were also identified. However, findings from the HPS2-THRIVE study could be used to strengthen the existing warnings in acipimox product information about use with statins.

[1] More information can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Referrals/Tredaptive, Pelzont and Trevaclyn.

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Overall, the data available on acipimox is limited compared to other currently available treatments for lipid disorders and evidence of effectiveness is based on changes in blood lipids, especially triglycerides, rather than reduction in risk of cardiovascular (heart and circulation) disorders. However, the side effects are well understood through many years of use.

The PRAC concluded that acipimox continues to have a role as an additional or alternative treatment to reduce triglycerides in those forms of hyperlipoproteinaemia that involve high triglyceride levels (with or without increased cholesterol), in patients in whom lifestyle changes and use of other medicines such as fibrates and statins are not adequate. The PRAC therefore concluded that the marketing authorisations for acipimox-containing medicines should be amended accordingly across the EU. The Committee also recommended expanding the warnings in the product information concerning a possible increased risk of painful muscle damage when acipimox is used together with a statin.

The PRAC recommendation will be sent to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) at its meeting of 16-18 December 2013.[2]

More about the medicine

Acipimox is a substance closely related to nicotinic acid that has been available since 1984 as Olbetam and other invented names for the treatment of lipid disorders. In the EU, acipimox-containing medicines are currently marketed in Austria, Belgium, Denmark, Hungary, Italy, Luxembourg, the Netherlands and the United Kingdom.

Medicines containing nicotinic acid or related substances have been authorised in the EU via national procedures since the mid-1950s. 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. Nicotinic acid was also authorised in combination with laropiprant. Laropiprant has no effect on cholesterol but it reduces flushing, which is a known side effect of nicotinic acid.

More about the procedure

The review of nicotinic acid and its related substances acipimox and xantinol nicotinate was initiated on 27 February 2013 at the request of the Danish Health and Medicines Authority, under Article 31 of Directive 2001/83/EC. In July 2013 it was established that nicotinic acid and the related substance xantinol nicotinate were not currently marketed in the EU to treat lipid disorders (xantinol nicotinate is authorised in some EU countries for oral use as a vasodilator, a medicine that widens the blood vessels used to treat blood circulation problems) and the review was therefore restricted to acipimox only.

The review has been conducted by the Pharmacovigilance Risk Assessment Committee (PRAC). As the review only covers nationally authorised medicines, the PRAC recommendation will now be forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh, a body representing EU Member States, is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

If the CMDh position is agreed by consensus, the agreement will be directly implemented by the Member States where the medicines are authorised. Should the CMDh position be adopted by majority

[2] The companies that market acipimox have the right to ask for a re-examination of the PRAC recommendation within 15 days of receipt of the PRAC recommendation, which would delay the expected time of finalisation of this review.

vote, the CMDh position will be sent to the European Commission, for the adoption of an EU-wide legally binding decision.

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