European Medicines Agency

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EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)

TREVACLYN

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis of the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Trevaclyn?

Trevaclyn is a medicine containing two active substances: nicotinic acid (also known as niacin or vitamin B_3) and laropiprant. It is available as modified-release tablets. 'Modified-release' means that the two active substances are released at different rates from the tablet over a few hours.

What is Trevaclyn used for?

Trevaclyn is used in addition to diet and exercise in patients with dyslipidaemia (abnormally high levels of fat in the blood), particularly 'combined mixed dyslipidaemia' and 'primary hypercholesterolaemia'. Patients with combined mixed dyslipidaemia have high blood levels of 'bad' LDL cholesterol and triglycerides (a type of fat), and low levels of 'good' HDL cholesterol. Primary hypercholesterolaemia is when the levels of cholesterol in the blood are high. Primary means that the hypercholesterolaemia does not have any identifiable cause.
Trevaclyn is normally given together with a statin (the standard medicine used to reduce cholesterol) when the effectiveness of a statin taken alone is inadequate. Trevaclyn is used on its own only in patients who cannot take statins.
The medicine can only be obtained with a prescription.

How is Trevaclyn used?

The starting dose of Trevaclyn is one tablet once a day for four weeks, after which the dose is increased to two tablets once a day. It is taken by mouth, with food, in the evening or before going to bed. The tablets must be swallowed whole, and should not be split, broken, crushed or chewed. Trevaclyn is not recommended for use in children under 18 years of age because of a lack of information on its safety and effectiveness in this group. It should be used with caution in patients who have problems with their kidneys and should not be used in patients with liver problems.

How does Trevaclyn work?

The two active substances in Trevaclyn, nicotinic acid and laropiprant, have different modes of action. Nicotinic acid is a naturally occurring substance that is used in low doses as a vitamin. 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).

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Flushing due to nicotinic acid is thought to occur because of the release of a substance called 'prostaglandin D2' (PGD_2) from cells in the skin, which dilates (widens) the blood vessels in the skin. Laropiprant blocks the receptors to which PGD_2 normally attaches. When the receptors are blocked, PGD_2 cannot dilate the vessels in the skin, reducing the frequency and intensity of flushing.
In Trevaclyn tablets, laropiprant is in one of the layers, and the other layer contains nicotinic acid. When the patient takes the tablet, laropiprant is released first into the bloodstream and blocks the PGD_2 receptors. The nicotinic acid is released more slowly from the other layer and has its effect as a fat-modifying agent.

How has Trevaclyn been studied?
The effects of Trevaclyn were first tested in experimental models before being studied in humans. Trevaclyn was studied in four main studies in patients with hypercholesterolaemia or mixed dyslipidaemia.
Two studies looked at the effectiveness of Trevaclyn in modifying blood fat levels. The first study compared the effectiveness of Trevaclyn with that of nicotinic acid alone or placebo (a dummy treatment) in reducing the levels of LDL cholesterol in a total of 1,613 patients. This study also looked at the symptoms of flushing using a specially designed questionnaire.
The second study compared the combination of Trevaclyn and simvastatin (a statin) with Trevaclyn alone or simvastatin alone in 1,398 patients. The main measure of effectiveness was the change in the blood levels of LDL cholesterol after 12 weeks.
The third and fourth studies looked at the effectiveness of laropiprant in reducing the flushing caused by nicotinic acid. They included a total of 2,349 patients who were taking either Trevaclyn or nicotinic acid. Flushing was measured using the flushing symptom questionnaire.

What benefit has Trevaclyn shown during the studies?
Trevaclyn was effective in reducing the blood levels of LDL cholesterol. In the first study, LDL cholesterol levels were reduced by 19% in patients taking Trevaclyn, compared with 1% in those taking placebo. The second study showed that the LDL cholesterol levels were further reduced when Trevaclyn was taken with simvastatin (48% reduction), compared with Trevaclyn alone (17% reduction) or simvastatin alone (37% reduction).
Adding laropiprant to nicotinic acid reduced the symptoms of flushing caused by nicotinic acid. In the first and third studies, fewer patients taking Trevaclyn reported moderate, severe or extreme flushing than patients taking nicotinic acid alone. In the fourth study, flushing was seen on fewer days in patients taking Trevaclyn than in those taking nicotinic acid alone.

What is the risk associated with Trevaclyn?
The most common side effect with Trevaclyn (seen in more than 1 patient in 10) is flushing. For the full list of all side effects reported with Trevaclyn, see the Package Leaflet.
Trevaclyn should not be used in people who may be hypersensitive (allergic) to nicotinic acid, laropiprant or any of the other ingredients. It should also not be used in patients who have problems with their liver, an active stomach ulcer or bleeding from an artery.

Why has Trevaclyn been approved?
The Committee for Medicinal Products for Human Use (CHMP) decided that Trevaclyn's benefits are greater than its risks for the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia and in patients with primary hypercholesterolaemia. The Committee recommended that Trevaclyn be given marketing authorisation.

Other information about Trevaclyn:
The European Commission granted a marketing authorisation valid throughout the European Union for Trevaclyn to Merck Sharp & Dohme Ltd. on 3 July 2008.

The full EPAR for Trevaclyn can be found here.

This summary was last updated in 05-2008.