Repatha
evolocumab

This is a summary of the European public assessment report (EPAR) for Repatha. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Repatha.

For practical information about using Repatha, patients should read the package leaflet or contact their doctor or pharmacist.

What is Repatha and what is it used for?

Repatha is a medicine used to treat:

- adults with primary hypercholesterolaemia (high blood cholesterol levels, in particular of LDL-cholesterol or 'bad cholesterol'). Primary means that the disease is generally the result of a genetic abnormality. Primary hypercholesterolaemia includes heterozygous familial (when the genetic abnormality is inherited from one parent) and heterozygous non-familial disease (when the genetic abnormality arises spontaneously without a family history). Repatha is also used to treat mixed dyslipidaemia (abnormal levels of fats in blood, including high levels of LDL-cholesterol). Repatha is to be used together with a low-fat diet, in the following cases:
  - in combination with a statin (another type of cholesterol-lowering medicine), or a statin plus other fat-lowering medicines, in patients whose blood fat levels are not lowered adequately with the maximum dose of the statin;
  - alone or in combination with other fat-lowering medicines in patients who cannot tolerate or cannot be given statins.
- adults and children aged 12 years and over who have homozygous familial hypercholesterolaemia (a severe form of hypercholesterolaemia caused by a genetic abnormality inherited from both parents). Repatha is to be used in combination with other fat-lowering medicines.
Repatha contains the active substance evolocumab.

**How is Repatha used?**

Before starting treatment with Repatha, other causes of excess cholesterol and abnormal fat levels in blood should be ruled out.

Repatha is available as a solution for injection in pre-filled syringes (140 mg), pre-filled pens (140 mg) and cartridges (420 mg). The cartridges are to be used together with an automated dosing device called a mini-doser. The injection is given under the skin of the abdomen, thigh or upper arm.

The recommended dose for adults with primary disease is either 140 mg every two weeks or 420 mg (the contents of three pre-filled syringes or one cartridge) once a month.

For adults and children aged 12 years and above with homozygous familial hypercholesterolaemia, the initial recommended dose is 420 mg once a month. If the desired response is not achieved after 12 weeks of treatment, the dose can be increased up to 420 mg every two weeks.

The medicine can only be obtained with a prescription. Patients can self-administer the medicine once they have been properly trained.

For more information, see the package leaflet.

**How does Repatha work?**

The active substance in Repatha, evolocumab, is a monoclonal antibody (a type of protein) that has been designed to recognise and attach to an enzyme called 'PCSK9'. This enzyme attaches to cholesterol receptors on the surface of liver cells and causes these receptors to be absorbed and broken down inside the cells. These receptors control blood levels of cholesterol, especially LDL-cholesterol, by removing it from the bloodstream. By attaching and blocking PCSK9, Repatha prevents the receptors from being broken down inside cells and therefore increases the number of these receptors on the cell surface, where they can attach to LDL-cholesterol and remove it from the bloodstream. This helps to reduce the amount of cholesterol in the blood. Repatha also helps to reduce other fatty substances from blood in patients with mixed dyslipidaemia.

**What benefits of Repatha have been shown in studies?**

In primary hypercholesterolaemia and mixed dyslipidaemia, Repatha was studied in 9 main studies involving around 7,400 adult patients, including patients with heterozygous familial disease. Some of the studies looked at Repatha taken on its own, while others studied Repatha in combination with other fat-lowering medicines, including patients on the maximum recommended doses of statins. Some studies compared Repatha with placebo (a dummy treatment) and others to another medicine (ezetimibe). These studies found a substantial reduction in blood levels of LDL-cholesterol (around 60 to 70% more than placebo, and of around 40% more than ezetimibe) from week 10 to week 12 of the study and at the end of 12 weeks.

In homozygous familial hypercholesterolaemia, Repatha was studied in 2 main studies involving 155 patients, which included 14 children older than 12 years. One of these studies showed that Repatha given together with other fat-lowering medicines reduced fat levels in the blood after 12 weeks of treatment (around 15 to 32% more than placebo given on top of other fat-lowering medicines). A second study showed that long-term use of Repatha achieved a sustained reduction of fat levels in the blood in these patients during 28 weeks of treatment.
**What are the risks associated with Repatha?**

The most common side effects with Repatha (which may affect up to 1 in 100 people) are nasopharyngitis (inflammation of the nose and throat), upper respiratory tract infection (nose and throat infection), back pain, joint pain, flu and nausea (feeling sick). For the full list of side effects and restrictions, see the package leaflet.

**Why is Repatha approved?**

The Agency’s Committee for Medicinal Products for Human Use (CHMP) decided that Repatha’s benefits are greater than its risks and recommended that it be approved for use in the EU. The Committee noted that across all studies in patients with primary hypercholesterolaemia and mixed dyslipidaemia, Repatha showed an important reduction in LDL-cholesterol levels, which is a known risk factor for cardiovascular disease. It is not yet known, however, whether Repatha will reduce cardiovascular disease. The Committee also noted that for patients with homozygous familial disease there are limited treatment options, and these patients have a higher risk of cardiovascular disease. In this population, including some children above 12 years, Repatha showed a consistent reduction in LDL-cholesterol levels beyond what can be achieved with existing fat-lowering medicines. With regard to safety, the Committee noted an acceptable safety profile and did not identify any substantial safety issue.

**What measures are being taken to ensure the safe and effective use of Repatha?**

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Repatha have been included in the summary of product characteristics and the package leaflet.

**Other information about Repatha**

The European Commission granted a marketing authorisation valid throughout the European Union for Repatha on 17 July 2015.

The full EPAR for Repatha can be found on the Agency’s website: [ema.europa.eu/Find medicine/Human medicines/European public assessment reports](http://ema.europa.eu/Find medicine/Human medicines/European public assessment reports). For more information about treatment with Repatha, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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