European Medicines Agency

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EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)

REFLUDAN

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 Refludan?
Refludan is a powder that is dissolved to make up a solution for injection or infusion (drip into a vein). It contains the active substance lepirudin.

What is Refludan used for?
Refludan is used to prevent blood clotting. It is used in adults with heparin-induced thrombocytopenia (HIT, a type of allergy to heparin that causes a lack of platelets in the blood or clots in the blood vessels) and who have thromboembolic disease (abnormal development of blood clots) that needs injected anti-clotting treatment, usually heparin. The diagnosis must be confirmed using specific tests, such as the heparin-induced platelet aggregation assay (HIPAA) test.
The medicine can only be obtained with a prescription.

How is Refludan used?
Treatment with Refludan should be started by a doctor who has experience in the treatment of coagulation (clotting) disorders.
The recommended dose is 0.4 mg per kilogram body weight as a single injection into a vein, followed by a continuous infusion at a dose of 0.15 mg/kg per hour for two to 10 days, or longer if needed. The doses need to be reduced in patients with kidney problems.

How does Refludan work?
Refludan is an antithrombotic medicine (a medicine that prevents the blood from clotting). The active substance in Refludan, lepirudin, is nearly identical to hirudin, the anti-clotting substance produced by leeches. Lepirudin specifically blocks a substance called thrombin, which is central for the complete process of blood clotting. By blocking thrombin, Refludan greatly reduces the risk of blood clots forming, preventing subsequent damage.
Lepirudin is produced by a method known as 'recombinant DNA technology': it is made by a cell that has received a gene (DNA), which makes it able to produce lepirudin.

How has Refludan been studied?
Refludan has been studied in two main studies involving 198 patients, 125 of whom had HIT and thromboembolic disease. The studies looked at the numbers of patients who died, had an amputation, and had new thromboembolic (clotting) complications. The studies did not compare Refludan with

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any other treatments, so the results were judged against historical controls (the results expected in untreated patients, based on past studies).

What benefit has Refludan shown during the studies?
During the study period, 9% of the patients died (11 out of 125), 6% had amputations (7 out of 125) and 10% had new thromboembolic complications (12 out of 125). In the comparison with historical controls, the two trials taken together showed a significant benefit of Refludan on the rate of new thromboembolic complications and a trend towards increased survival.

What is the risk associated with Refludan?
As with other antithrombotic drugs, the most common side effect with Refludan (seen in more than 1 patient in 10) is bleeding. Bleeding leading to death occurs in around 1 patient in 100. For the full list of all side effects reported with Refludan, see the Package Leaflet.
Refludan should not be used in people who may be hypersensitive (allergic) to lepirudin, any other hirudin derivative, or any of the other ingredients. It must not be used in patients who are pregnant or breast-feeding. Its use is not advisable in patients who are bleeding or are at risk of bleeding because of a recent biopsy, stroke or major surgery, or because they are over the age of 65 years, among other reasons. See the Package Leaflet for the full list of restrictions.
Some patients can have a serious allergic shock when they receive Refludan for a second time. Doctors should be very careful when re-exposing a patient to the medicine.

Why has Refludan been approved?
As the disease is very severe and there are no other effective treatments approved, the Committee for Medicinal Products for Human Use (CHMP) decided that Refludan's benefits are greater than its risks for the treatment of patients with HIT and thromboembolic disease. The Committee recommended that Refludan be given marketing authorisation.

Other information about Refludan:
The European Commission granted a marketing authorisation valid throughout the European Union for Refludan on 13 March 1997. The marketing authorisation was renewed on 13 March 2002 and on 13 March 2007. The marketing authorisation holder is Celgene Europe Ltd.

The full EPAR for Refludan is available here.

This summary was last updated in 04-2009.