EMA/319898/2023
EMEA/H/C/004178

Refixia *(nonacog beta pegol)*

An overview of Refixia and why it is authorised in the EU

What is Refixia and what is it used for?

Refixia is a medicine used to treat and prevent bleeding in patients with haemophilia B, an inherited bleeding disorder caused by the lack of factor IX, a protein needed to produce blood clots to stop bleeding.

Refixia contains the active substance nonacog beta pegol.

How is Refixia used?

Refixia can only be obtained with a prescription and treatment should be under the supervision of a doctor who has experience in the treatment of haemophilia.

Refixia is given as an injection into a vein. The dose and frequency of treatment depend on whether Refixia is used to treat or prevent bleeding or to reduce bleeding during surgery, the extent and location of the bleed, and the patient's bodyweight.

Patients or their carers may be able to inject Refixia themselves at home once they have been trained appropriately. For full details, see the package leaflet.

For more information about using Refixia, see the package leaflet or contact your doctor or pharmacist.

How does Refixia work?

Patients with haemophilia B lack factor IX, a protein needed for normal clotting of the blood, and as a result, they bleed readily. The active substance in Refixia, nonacog beta pegol, works in the body in the same way as human factor IX. It replaces the missing factor IX, thereby helping the blood to clot and giving temporary control of bleeding.

What benefits of Refixia have been shown in studies?

Refixia has been shown to be effective at both treating bleeding episodes and keeping the number of episodes low.

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In a study involving 74 adults and adolescents aged 13 or above, 29 patients given Refixia as a weekly preventive treatment had around 1 bleeding episode a year, and 15 patients given Refixia for treating bleedings 'on demand' had around 16 bleeding episodes a year. In addition, when bleeding did occur, Refixia was rated excellent or good at treating around 92% of bleeding episodes. 87% of bleeding episodes resolved with one injection of Refixia.

In the second study in 25 children aged below 13 years previously treated with other factor IX products, all patients were given Refixia as a weekly preventive treatment. After one year of treatment, patients had around 1 bleeding episode per year. Refixia was rated excellent or good at treating around 93% of bleeding episodes. Around 86% of bleeding episodes resolved with one injection. The study also provided data on the long-term use of Refixia. During up to 8 years of treatment with Refixia, the average yearly bleeding rate was 0.9 bleeds per year. Refixia was rated excellent or good at treating around 89% of bleeding episodes. Around 82% of bleeding episodes resolved with one injection of Refixia.

In a third study in 50 children aged below 7 years who were previously not treated with other factor IX products, Refixia was given as a weekly preventive treatment. During up to 6 years of treatment with Refixia, the average yearly bleeding rate was 0.7 bleeds per year. Refixia was rated excellent or good at treating around 96% of bleeding episodes. Around 91% of bleeding episodes resolved with one injection of Refixia.

Results from both studies in children also showed that after around 6 years of treatment with Refixia, patients achieved stable factor IX levels that were in the range expected for those with mild haemophilia.

What are the risks associated with Refixia?

For the full list of side effects and restrictions with Refixia, see the package leaflet.

Hypersensitivity (allergic) reactions are uncommon with Refixia (may affect up to 1 in 100 patients) and may include: swelling, burning and stinging at the injection site, chills, flushing, itchy rash, headache, hives, low blood pressure, lethargy, nausea and vomiting, restlessness, a fast heartbeat, tightness of the chest and wheezing. In some cases, these reactions can become severe.

Some patients taking factor IX medicines may develop inhibitors (antibodies) against factor IX, causing the medicine to stop working and resulting in a loss of bleeding control. Factor IX medicines can also potentially cause problems due to the formation of blood clots in the blood vessels.

Refixia must not be used in patients allergic to nonacog beta pegol or any of the ingredients of the medicine, nor in those with known allergy to hamster proteins.

Why is Refixia approved?

The European Medicines Agency decided that Refixia's benefits are greater than its risks and recommended that it be approved for use in the EU.

Studies have shown that Refixia is effective at preventing and treating bleeding episodes in patients with haemophilia B and its safety is comparable to that of other factor IX products. However, part of the active substance in Refixia (called PEG) may accumulate in the body, including in a structure in the brain called choroid plexus, following long-term treatment.

Long-term use of Refixia in children below 13 years of age resulted in a low yearly bleeding rate. In addition, Refixia was considered to provide a protective effect against bleeding episodes by generating

stable factor IX levels in children below 13 years who were given the medicine to prevent bleeding. Refixia was previously not authorised for children below 12 years of age because of concerns about the accumulation of PEG in young children. Comprehensive data from studies, including data on long-term use, has not shown any link with side effects on the nervous system due to the accumulation of PEG.

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

The company that markets Refixia will conduct a study to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other organs.

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

Other information about Refixia

Refixia received a marketing authorisation valid throughout the EU on 2 June 2017.

Further information on Refixia can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/refixia

This overview was last updated in 07-2023.