Revolade
eltrombopag

This document is a summary of the European Public Assessment Report (EPAR) for Revolade. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Revolade.

What is Revolade?

Revolade is medicine that contains the active substance eltrombopag. It is available as tablets (12.5, 25, 50 and 75 mg). It is also available as a powder (25 mg) to prepare a suspension to be taken by mouth.

What is Revolade used for?

Revolade is used for the treatment of:

- long-term immune (idiopathic) thrombocytopenic purpura (ITP), a disease in which the patient’s immune system destroys the platelets (components in the blood that help it to clot). Patients with ITP have low platelet counts in the blood (thrombocytopenia) and are at risk of bleeding. Revolade is used in patients aged 1 year and above who do not respond to treatment with medicines such as corticosteroids or immunoglobulins;
- thrombocytopenia in adult patients with chronic (long-term) hepatitis C, a disease of the liver caused by infection with the hepatitis C virus, when the severity of thrombocytopenia is preventing antiviral therapy;
- acquired severe aplastic anaemia (a disease in which the bone marrow does not make enough blood cells) in adult patients. Revolade is used in patients who did not respond to or had received multiple courses of immunosuppressive therapy (medicines that lower the body’s immune defences) and cannot receive haematopoietic (blood) stem cell transplantation.

The medicine can only be obtained with a prescription.
How is Revolade used?

Treatment with Revolade should be started and supervised by a doctor who has experience in treating blood diseases or chronic hepatitis C and its complications.

In adults with chronic ITP or severe aplastic anaemia, the recommended starting dose is 50 mg once a day, except in patients of East Asian descent (such as Japanese, Chinese, Taiwanese or Korean) where it should be 25 mg once a day. After treatment has started, the dose should be adjusted for each patient with the aim of keeping the level of platelets high enough to prevent bleeding (above 50,000 platelets per microlitre). The daily dose should not exceed 75 mg in ITP patients and 150 mg in severe aplastic anaemia patients. Platelet levels should be monitored regularly and the dose of Revolade should be adjusted if needed. Doctors should also periodically assess patients with chronic ITP who still have a spleen to see if they require surgery.

In children with ITP, the daily recommended dose is 25 mg for children aged 1 to 5 years, and 50 mg for children aged 6 to 17 years, except in patients of East Asian descent (such as Japanese, Chinese, Taiwanese or Korean) where it should be 25 mg once a day.

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How does Revolade work?

In the body, a hormone called ‘thrombopoietin’ stimulates the production of platelets by attaching to certain receptors in the bone marrow. The active substance in Revolade, eltrombopag, attaches to and stimulates the same receptors as thrombopoietin. This leads to an increased production of platelets.

How has Revolade been studied?

For the treatment of chronic ITP in adults, Revolade was compared with placebo (a dummy treatment) in two main studies involving a total of 311 adults with chronic ITP. The patients had previously been treated but the treatments had not worked or the disease had come back. All of the patients had a platelet count of less than 30,000 per microlitre at the start of the studies. In the first study, the main measure of effectiveness was the number of patients whose platelet count had increased to at least 50,000 cells per microlitre after six weeks. In the second study, it was the number of patients who had a platelet count between 50,000 and 400,000 per microlitre during six months of treatment.

In children with chronic ITP, Revolade was compared with placebo in one main study involving a total of 92 children between 1 and 17 years of age who had previously received treatment for ITP. This study lasted 13 weeks and looked at the proportion of patients whose platelet count had increased to at least 50,000 cells per microlitre for at least 6 out of 8 weeks, between week 5 to 12 of the study in the absence of rescue medication. The study had also an extension phase, in which all patients received Revolade. This phase looked at the long-term effect on platelet levels.
For the treatment of thrombocytopenia associated with hepatitis C, two main studies involving a total of 1,441 adults were carried out. These compared Revolade with placebo for allowing the starting and maintenance of antiviral treatment in patients with hepatitis C whose platelet count was initially too low to allow starting such treatment (less than 75,000 per microlitre). In both studies, the main measure of effectiveness was the number of patients whose blood tests did not show any sign of hepatitis C virus 6 months after the end of treatment.

For the treatment of severe aplastic anaemia, Revolade was studied in 43 patients and it was not compared with any other medicine. The main measure of effectiveness was the number of patients who responded to Revolade (whose platelet, red or white blood cell count remained above pre-set levels) after 12 or 16 weeks of treatment.

**What benefit has Revolade shown during the studies?**

In the treatment of adults with chronic ITP, Revolade was more effective than placebo. In the first ITP study, 59% of the patients who took Revolade (43 out of 73) had a platelet count of at least 50,000 per microlitre after six weeks, compared with 16% of those who took placebo (6 out of 37). In the second ITP study, patients taking Revolade were around eight times more likely than those taking placebo to reach a platelet count of between 50,000 and 400,000 per microlitre during the six months of treatment.

Revolade was also more effective than placebo in children with ITP, with around 40% of the patients who took Revolade (25 out of 63) having a platelet count of at least 50,000 per microlitre for at least 6 of 8 weeks between weeks 5 to 12 of the study period, compared with around 3% of those who took placebo (1 out of 29). Revolade was also effective at maintaining adequate levels of platelets in the extension phase of the study.

In the treatment of thrombocytopenia associated with hepatitis C, a higher proportion of patients who took Revolade tested negative for hepatitis C, compared with those who took placebo (23% versus 14% in the first study, and 19% versus 13% in the second study).

In severe aplastic anaemia, 40% of patients (17 out of 43) responded to treatment after 12 weeks, and 65% of responders (11 out of 17) either had a platelet count increase of at least 20,000 cells per microliter or had a platelet count that was stable without need for blood transfusions. Preliminary data from a supportive study are consistent with the result of the main study, with 46% of patients responding to treatment after 12 weeks.

**What is the risk associated with Revolade?**

The most common side effects with Revolade in adults with chronic ITP and hepatitis C (seen in more than 1 patient in 10) are headache, anaemia (low red blood cell counts), decreased appetite, insomnia (difficulty sleeping), cough, nausea (feeling sick), diarrhoea, pruritus (itching), alopecia (hair loss), myalgia (muscle pain), pyrexia (fever), fatigue (tiredness), influenza (flu)-like illness, asthenia (weakness), chills and peripheral oedema (swelling, especially of the ankles and feet). In addition, in children with ITP the most common side effects also included colds, nasopharyngitis (inflammation of the nose and throat), rhinitis (inflammation of the lining of the nose), pain in the tummy or in the mouth and throat, toothache, rash, runny nose and abnormal blood levels of certain liver enzymes (AST).

In adults with severe aplastic anaemia the most common side effects included headache, dizziness, insomnia, cough, dyspnoea (difficulty breathing), pain in the tummy or in the mouth and throat,
nausea, diarrhoea, joint pain, muscle spasms, pain in limbs, fatigue, fever, ecchymosis (discoloration of the skin resulting from bleeding underneath), abnormal blood levels of certain liver enzymes and runny nose.

There is also an increased risk of liver problems and thromboembolic complications (problems with clots in blood vessels) in patients with thrombocytopenia and advanced chronic hepatitis C who are treated with a medicine called interferon and Revolade. In these patients Revolade should only be used if clinically indicated and patients should then be closely monitored. Bleeding can also come back after the medicine is stopped. For the full list of restrictions and side effects with Revolade, see the package leaflet.

**Why has Revolade been approved?**

The CHMP decided that Revolade’s benefits are greater than its risks and recommended that it be given marketing authorisation.

**What measures are being taken to ensure the safe use of Revolade?**

A risk management plan has been developed to ensure that Revolade is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Revolade, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that markets Revolade will ensure that doctors in all Member States who will prescribe the medicine are provided with educational materials reminding them how the medicine should be used and of the medicine’s possible side effects such as liver problems, thromboembolic complications and the recurrence of bleeding.

**Other information about Revolade:**

The European Commission granted a marketing authorisation valid throughout the European Union for Revolade on 11 March 2010.

The full EPAR for Revolade can be found on the Agency’s website: [ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports](https://ema.europa.eu). For more information about treatment with Revolade, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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