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Refusal of a change to the marketing authorisation for Revolade (eltrombopag)

Re-examination confirms refusal

After re-examining its initial opinion, the European Medicines Agency has confirmed its recommendation to refuse a change to the marketing authorisation for the medicine Revolade. The change concerned an extension of indication to add treatment of previously untreated patients with severe aplastic anaemia from 12 years of age who cannot have stem cell transplantation (a procedure where the patient's bone marrow is cleared of cells and replaced by stem cells from a donor).

The Agency issued this opinion on 17 October 2019, after concluding the re-examination. The Agency had issued its initial opinion on 27 June 2019. The company that applied for the change to the authorisation was Novartis Europharm Limited.

What is Revolade and what is it used for?

Revolade is a medicine used to treat:

- patients from 1 year of age with immune thrombocytopenia (when the patient's immune system destroys platelets, putting the patient at risk of bleeding), if other usual treatment has not worked;
- thrombocytopenia in adults with chronic (long-term) hepatitis C when the disease prevents the use of certain types of hepatitis C treatment;
- adults with severe aplastic anaemia (when the bone marrow does not make enough blood cells or platelets), if immunosuppressive therapy (medicines that lower the body's immune defences) has not worked and the patient cannot receive bone marrow transplantation.

Revolade has been authorised in the EU since March 2010. It contains the active substance eltrombopag and is available as tablets and as a powder to make up a liquid to take by mouth.

Further information on Revolade's current uses can be found on the Agency's website: ema.europa.eu/en/medicines/human/EPAR/revolade.

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What change had the company applied for?

The company originally applied for an extension of indication to add treatment of severe aplastic anaemia in previously untreated adults and children aged from 2 years. During the initial evaluation the company then changed the proposed indication to include only patients above 12 years of age who cannot have stem cell transplantation.

How does Revolade work?

In the body, a hormone called thrombopoietin stimulates the production of platelets and some types of blood cells by attaching to certain receptors (targets) in the bone marrow. The active substance in Revolade, eltrombopag, likewise attaches to and stimulates the thrombopoietin receptors. This increases the production of platelets and some other blood cells, improving platelet and blood cell counts.

What did the company present to support its application?

The company provided data from a study involving 153 patients from 3 years of age with severe aplastic anaemia who had not previously received immunosuppressive therapy. In the study, Revolade was combined with immunosuppressants that are used for treating aplastic anaemia. Treatment was considered successful if the patient's white blood cell and platelet counts and haemoglobin rose to satisfactory levels.

What were the main reasons for refusing the change to the marketing authorisation?

The design of the study was not considered adequate to show that Revolade is effective for treating severe aplastic anaemia in previously untreated patients. The study did not make a direct comparison between Revolade combined with immunosuppressant treatment and immunosuppressant treatment alone. Instead, the comparison was with patients treated with immunosuppressants in other studies. Such comparison prevents drawing reliable conclusions on the effect of Revolade when added to immunosuppressants. Moreover, adequate amount of data were not available on the use of Revolade in children.

Therefore, the Agency's opinion was that the balance of benefits and risks of Revolade in the initial treatment of severe aplastic anaemia could not be established. Hence, the Agency recommended refusing the change to the marketing authorisation. The initial refusal was confirmed after re-examination.

Does this refusal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients who are receiving Revolade for initial treatment of severe aplastic anaemia in clinical trials or in compassionate use programmes.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.

What is happening with Revolade for treatment of other diseases?

There are no consequences for Revolade in its authorised uses.