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EPAR summary for the public

Rydapt

midostaurin

This is a summary of the European public assessment report (EPAR) for Rydapt. 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 Rydapt.

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

What is Rydapt and what is it used for?

Rydapt is a cancer medicine used to treat adults with newly diagnosed acute myeloid leukaemia (AML), a cancer of white blood cells. It is used with other cancer medicines (chemotherapy) initially and on its own once the chemotherapy is completed if the disease has responded to treatment. Rydapt is only given when the AML has a particular genetic change called an FLT3 mutation.

Rydapt is also used on its own in adults with the following disorders of a type of white blood cell known as mast cell: aggressive systemic mastocytosis, systemic mastocytosis associated with a haematological neoplasm (blood cancer), and mast cell leukaemia.

Because the number of patients with these diseases is low, they are considered ‘rare’, and Rydapt was designated an ‘orphan medicine’ (a medicine used in rare diseases) on various dates (see below).

Rydapt contains the active substance midostaurin.

How is Rydapt used?

Rydapt can only be obtained with a prescription and treatment should be started by a doctor experienced in the use of cancer medicines. Rydapt is available as capsules containing 25 mg of midostaurin. The usual starting dose is 50 mg (two capsules) twice a day for AML, on days 8 to 21 of a 28-day treatment cycle, and then every day once the disease has responded. Treatment is continued

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for up to 12 cycles depending on how patients respond. For mast cell disorders, the starting dose is 100 mg (four capsules) twice daily; treatment is continued for as long as the patient benefits. If a patient develops certain severe side effects, the doctor may decide to reduce subsequent doses or delay or stop treatment.

For further information, see the package leaflet.

How does Rydapt work?

The active substance in Rydapt, midostaurin, is a 'tyrosine kinase inhibitor'. This means that it blocks the action of certain enzymes known as receptor tyrosine kinases. In patients with an FLT3 mutation, an abnormal form of the FLT3 tyrosine kinase stimulates the survival and growth of AML cells. By blocking the abnormal FLT3 enzyme, Rydapt helps to bring about the death of the abnormal cells and control the spread of the cancer. Rydapt also blocks a mutated form of another enzyme, KIT kinase, which plays an important role in stimulating the abnormal growth of mast cells in patients with mast cell disorders.

What benefits of Rydapt have been shown in studies?

Rydapt has been shown to improve survival in patients with AML associated with an FLT3 mutation. One main study, involving 717 such patients, compared Rydapt with placebo (a dummy treatment) initially as an addition to other cancer medicines, followed by treatment with Rydapt or placebo alone in those whose disease responded. About 51% of those given Rydapt and 43% of those given placebo were still alive after 5 years.

Another main study involving 116 patients with mast cell disorders also showed benefit. The study looked at the response to Rydapt treatment in patients with aggressive systemic mastocytosis, systemic mastocytosis associated with blood cancer, or mast cell leukaemia. Overall, using the most stringent, up-to-date criteria, the disease responded to treatment in about 28% of patients (32 of 113). When looked at separately the response rate was highest (60%) in those with aggressive systemic mastocytosis.

What are the risks associated with Rydapt?

When used to treat AML, the most common side effects with Rydapt (which may affect more than 1 in 10 people) are febrile neutropenia (fever and low white blood cell count, seen in nearly all patients), exfoliative dermatitis (inflamed, peeling skin), vomiting, headache, petechiae (tiny blood spots under the skin) and fever. The most frequent severe side effects were febrile neutropenia, lymphopenia (low counts of lymphocytes, a particular type of white blood cell), infections at the site of a catheter (a tube inserted in a vein), exfoliative dermatitis, high blood sugar and nausea (feeling sick).

When used for mast cell disorders, the commonest side effects (affecting one third or more of all patients) were nausea, vomiting, diarrhoea, peripheral oedema (swelling of the ankles and feet) and tiredness. The commonest severe side effects were tiredness, sepsis (blood poisoning), pneumonia (lung infection), febrile neutropenia and diarrhoea.

For the full list of all side effects reported with Rydapt, see the package leaflet.

Rydapt must not be given to patients taking certain other medicines that affect the way it is handled in the body. For the full list of restrictions, see the package leaflet.

Why is Rydapt approved?

Rydapt has been shown to be of benefit in patients with AML associated with an FTL3 mutation. The safety of the medicine was acceptable in such a severe condition and was considered manageable.

In mast cell disorders there was also important evidence of effectiveness. Although Rydapt had not been compared with other treatments, given the rarity of the conditions and the unmet medical need of patients who have them, the clinical benefits were clear, and the adverse effects acceptable.

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

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

The company that markets Rydapt will complete three further studies to provide the Agency with evidence to support the effectiveness of the medicine in elderly patients with AML.

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

Other information about Rydapt

The European Commission granted a marketing authorisation valid throughout the European Union for Rydapt on 18 September 2017.

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

The summaries of the opinion of the Committee for Orphan Medicinal Products for Rydapt can be found on the Agency's website:

acute myeloid leukaemia

mastocytosis.

This summary was last updated in 08-2017.