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Recommendation for maintenance of orphan designation at the time of marketing authorisation

Rydapt (midostaurin) for the treatment of acute myeloid leukaemia and mastocytosis

On 25 July 2017, the Committee for Orphan Medicinal Products (COMP) completed a review of the designations EU/3/04/214 and EU/3/10/765 for Rydapt (midostaurin) as an orphan medicinal product for the treatment of acute myeloid leukaemia (AML) and mastocytosis. The COMP assessed whether, at the time of marketing authorisation, the medicinal product still met the criteria for orphan designation. The Committee looked at the seriousness and prevalence of the conditions, and the existence of other methods of treatment. As other methods of treatment are authorised in the European Union (EU), the COMP also considered whether the medicine is of significant benefit to patients with AML and mastocytosis. The COMP recommended that the orphan designations of the medicine be maintained[1].

Life-threatening or long-term debilitating nature of the condition

The Committee for Medicinal Products for Human Use (CHMP) recommended the authorisation of Rydapt for:

- 'Acute myeloid leukaemia (AML)

  In combination with standard daunorubicin and cytarabine induction and high dose cytarabine consolidation chemotherapy, and for patients in complete response followed by Rydapt single agent maintenance therapy, for adult patients with newly diagnosed acute myeloid leukaemia (AML) who are FLT3 mutation positive

- Aggressive systemic mastocytosis

  As monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM AHN), or mast cell leukaemia (MCL)'

[1] The maintenance of the orphan designation at time of marketing authorisation would, except in specific situations, give an orphan medicinal product 10 years of market exclusivity in the EU. This means that in the 10 years after its authorisation similar products with the same therapeutic indication cannot be placed on the market.

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This falls within the scope of the product's designated orphan indications, which are: 'treatment of acute myeloid leukaemia' and 'treatment of mastocytosis'.

The COMP concluded that there had been no change in the seriousness of the conditions since the orphan designations in 2004 (AML) and 2010 (mastocytosis). AML and mastocytosis remain conditions that are progressive, debilitating in the long term and life threatening, particularly due to bone marrow failure.

Prevalence of the condition

The sponsor provided updated information on the prevalence of AML and mastocytosis based on data from European registries and the RARECARE database.

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of AML remains below the ceiling for orphan designation, which is 5 people in 10,000. At the time of the review of the orphan designation, the prevalence was estimated to be approximately 1 person in 10,000. This is equivalent to a total of around 52,000 people in the EU.

Similarly, the COMP also concluded that the prevalence of mastocytosis remains below the ceiling for orphan designation. At the time of the review of the orphan designation, the prevalence was estimated to be approximately 2.5 people in 10,000. This is equivalent to a total of around 129,000 people in the EU.

Existence of other methods of treatment

At the time of the review of the orphan designation, other treatments were authorised in the EU for the treatment of AML and mastocytosis. The main treatments for AML were chemotherapy (medicines to treat cancer) and haematopoietic (blood) stem-cell transplantation (a procedure where the patient's bone marrow is cleared of cells and replaced by stem cells to form new bone marrow that produces healthy blood cells). For mastocytosis, only treatments aimed at relieving the symptoms of mastocytosis were available. They included antihistamines to block the action of histamine produced by the mast cells.

Significant benefit of Rydapt

The COMP concluded that the claim of a significant benefit of Rydapt in AML is justified on the basis of studies showing improved survival compared with placebo (a dummy treatment) when the medicine was added to standard treatment in patients whose AML showed a particular genetic change known as an FLT3 mutation. Other available treatments do not specifically target this particular group, for whom Rydapt is considered to provide a clinically relevant advantage.

The COMP also concluded that the claim of a significant benefit of Rydapt in mastocytosis is justified on the basis of improved survival in patients with advanced systemic mastocytosis. Since the existing treatments only target specific symptoms of the disease, this was also considered to be a clinically relevant advantage.

Therefore, although other methods for the treatment of these conditions have been authorised in the EU, the COMP concluded that Rydapt is of significant benefit to patients affected by AML or mastocytosis.

Conclusions

Based on the data submitted and the scientific discussion within the COMP, the COMP considered that Rydapt still meets the criteria for designation as an orphan medicinal product and that it should remain in the Community Register of Orphan Medicinal Products.

More information on the COMP assessment can be found in the July 2017 COMP minutes.

Further information on Rydapt can be found in the European public assessment report (EPAR) on the Agency's website : ema.europa.eu/Find medicine/Human medicines/European public assessment reports.