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Committee for Orphan Medicinal Products

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

Iclusig (ponatinib) for the treatment of acute lymphoblastic leukaemia and chronic myeloid leukaemia

During its meeting of 16-17 April 2013, the Committee for Orphan Medicinal Products (COMP) reviewed the designations EU/3/09/715 and EU/3/09/716 for Iclusig (ponatinib[1]) as an orphan medicinal product for the treatment of acute lymphoblastic leukaemia and of chronic myeloid leukaemia. 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 satisfactory methods of treatment for patients with these conditions are authorised in the European Union (EU), the COMP also looked at the significant benefit of the product over existing treatments. The COMP recommended that the orphan designations of the medicine be maintained[2].

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

The Committee for Medicinal Products for Human Use (CHMP) recommended the authorisation of Iclusig for the treatment of adult patients with:

- chronic phase, accelerated phase, or blast phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib; who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation;
- Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to dasatinib; who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.

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

[1] Previously known as benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl].
[2] 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 a comparable therapeutic indication cannot be placed on the market.

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The COMP concluded that there had been no change in the seriousness of the conditions since the orphan designation in 2010. Despite the available treatments, ALL and CML remain long-term debilitating and life-threatening conditions.

Prevalence of the condition

The sponsor provided updated information on the prevalence of ALL and CML based on recent scientific literature and data from the Globocan 2008 database (which contains prevalence data for all types of leukaemia combined).

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of ALL and CML 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 in 10,000 people for ALL and 0.8 in 10,000 people for CML. In the EU, this is equivalent to a total of around 51,000 people for ALL and around 41,000 people for CML.

Existence of other satisfactory methods of treatment

At the time of the review of the orphan designation, several medicines were authorised in the EU for the treatment of ALL and CML, including imatinib, nilotinib and dasatinib, which are orphan medicines with a similar mechanism of action to Iclusig, known as 'tyrosine kinase inhibitors' (TKIs). In addition, bosutinib, another TKI orphan medicine, had been authorised in March 2013 for the treatment of CML in patients for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options. Haematopoietic stem cell transplantation (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow) was used in some patients.

Significant benefit over existing treatments

The COMP concluded that the claim of a significant benefit of Iclusig in the treatment of ALL and CML is justified because this medicine represents a valuable treatment option for those patients who are intolerant or resistant to treatment with currently approved TKIs. This is based on a study involving 449 patients with CML or Ph+ ALL who were intolerant or resistant to treatment with dasatinib or nilotinib. A subgroup of patients who were resistant to bosutinib were also included in the study. The study showed that treatment with Iclusig led to clinically relevant responses in all groups of patients. In addition, Iclusig was shown effective in patients who have the T315I mutation, for which treatment with currently available TKIs including bosutinib does not work.

Therefore, although other satisfactory methods for the treatment of this condition have been authorised in the EU, the COMP concluded that Iclusig is of significant benefit for patients affected by ALL or CML.

Conclusions

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

Further information on the current regulatory status of Iclusig 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.