



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

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

Ketoconazole HRA (ketoconazole) for the treatment of Cushing's syndrome

During its meeting of 7 to 9 October 2014, the Committee for Orphan Medicinal Products (COMP) reviewed the designation EU/3/12/965 for Ketoconazole HRA (ketoconazole) as an orphan medicinal product for the treatment of Cushing's syndrome. 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 condition, 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 Cushing's syndrome. The COMP recommended that the orphan designation of the medicine be maintained¹.

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

The Committee for Medicinal Products for Human Use (CHMP) recommended the authorisation of Ketoconazole HRA for: 'treatment of endogenous Cushing's syndrome in adults and adolescents above the age of 12 years'.

This falls within the scope of the product's designated orphan indication, which is: 'treatment of Cushing's syndrome'.

The COMP concluded that there had been no change in the seriousness of the condition since the orphan designation in 2012. Cushing's syndrome remains a condition that is debilitating in the long term and life threatening, particularly because of its complications, including diabetes, clotting disorders, muscular weakness, osteoporosis and mental problems.

Prevalence of the condition

The sponsor provided recent scientific literature on the prevalence of Cushing's disease. On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the

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 a comparable therapeutic indication cannot be placed on the market.



prevalence of Cushing's syndrome 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 still estimated to be approximately 0.9 people in 10,000. This is equivalent to a total of around 46,000 people in the EU.

Existence of other methods of treatment

At the time of the review of the orphan designation, the main treatment for Cushing's syndrome involved surgery to remove the tumour responsible for causing high cortisol levels. In patients in whom surgery does not work or cannot be used radiotherapy (treatment with radiation) or medicines can be used. Medicines authorised in the EU for the treatment of Cushing's syndrome to reduce the production of cortisol include metyrapone, mitotane and pasireotide.

Significant benefit of Ketoconazole HRA

The COMP concluded that the claim of a significant benefit of Ketoconazole HRA in Cushing's syndrome is justified on the basis of relevant data showing improved control of cortisol levels when ketoconazole was added to existing treatment of patients who were not completely controlled with other products currently authorised for the condition.

Therefore, although other methods for the treatment of this condition have been authorised in the EU, the COMP concluded that Ketoconazole HRA is of significant benefit to patients affected by Cushing's syndrome.

Conclusions

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

Further information on the current regulatory status of Ketoconazole HRA 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.