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EMA/COMP/68649/2014
Committee for Orphan Medicinal Products

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

Adempas (riociguat) for the treatment of pulmonary arterial hypertension including chronic thromboembolic pulmonary hypertension

During its meeting of 4 to 6 February 2014, the Committee for Orphan Medicinal Products (COMP) reviewed the designation EU/3/07/518 for Adempas (riociguat[1]) as an orphan medicinal product for the treatment of pulmonary arterial hypertension including chronic thromboembolic pulmonary hypertension. 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 satisfactory methods of treatment. As other methods of treatment for patients with this condition 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 designation 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 Adempas for:

- treatment of adult patients with WHO functional class II to III with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), or persistent or recurrent CTEPH after surgical treatment, to improve exercise capacity.
- treatment, as monotherapy or in combination with endothelin receptor antagonists, of adult patients with pulmonary arterial hypertension (PAH) with WHO functional class II to III, to improve exercise capacity.

This falls within the scope of the product's designated orphan indication, which is: 'treatment of pulmonary arterial hypertension including chronic thromboembolic pulmonary hypertension'.

[1] Previously known as methyl 4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4 b]pyridine-3-yl]-5-pyrimidinyl(methyl) carbamate.
[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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

The COMP concluded that there had been no change in the seriousness of the conditions since the orphan designation in 2007. PAH and CTEPH remain long-term debilitating and life threatening conditions that shorten patients' life expectancy because they may lead to heart failure.

Prevalence of the condition

The sponsor provided updated information on the prevalence of PAH and CTEPH from the scientific literature.

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of PAH and CTEPH 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 less than 2 people in 10,000. This is equivalent to a total of fewer than 102,000 people in the EU.

Existence of other satisfactory methods of treatment

At the time of the review of the orphan designation, surgery was a curative treatment for some patients with CTEPH. However, no medicines were authorised in the EU for the treatment of patients with inoperable CTEPH or those in whom CTEPH remained or returned after surgery.

For PAH, several medicines were authorised in the EU, including medicines belonging to the groups called prostanoids (such as epoprostenol, iloprost and treprostinil), PDE5 inhibitors (such as sildenafil and tadalafil), and endothelin receptor antagonists (such as bosentan and ambrisentan).

Significant benefit over existing treatments

The COMP concluded that the claim of a significant benefit of Adempas in the treatment of PAH and CTEPH is justified on the basis of data from 2 main clinical studies, one in 445 patients with PAH and the other in 262 patients with CTEPH. The study in PAH showed that Adempas significantly improved the distance patients could walk in six minutes (a valid measure of exercise capacity) when the medicine was used on its own or as an add-on to currently authorised treatments. Adempas works in a different way to currently authorised treatments, and the study with Adempas in PAH patients demonstrates the benefit of combining differently acting treatments.

Improvements in walking distance were also seen in the study in CTEPH, which included patients with inoperable disease and those in whom CTEPH remained or returned after surgery, for whom no alternative treatment is available.

Therefore, although other satisfactory methods for the treatment of PAH including CTEPH exist in the EU, the COMP concluded that Adempas is of significant benefit for patients with this condition.

Conclusions

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

Further information on the current regulatory status of Adempas 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.