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Press Office

Press release

Ketoconazole HRA recommended for approval in Cushing's syndrome

European Medicines Agency facilitates patients' access to a treatment of a rare hormonal disorder

The European Medicines Agency has recommended granting a marketing authorisation for Ketoconazole HRA (ketoconazole) in the treatment of Cushing's syndrome, a rare hormonal disorder sometimes called hypercortisolism. The Agency's Committee for Medicinal Products for Human Use (CHMP) evaluated the medicine under accelerated assessment, a regulatory tool meant to help speed up patients' access to new medicines where there is an unmet medical need.

Cushing's syndrome is characterised by an excess of the hormone cortisol in the blood, which may be caused by a tumour. In 2012, it was estimated that the disease affected approximately 46,000 people in the European Union (EU). Cushing's syndrome is a long-lasting disease that can be life-threatening because of its complications, including diabetes, high blood pressure and depression.

Treatment options currently available in the EU include surgery to remove the tumour responsible for the high cortisol levels, radiotherapy as well as several medicines that reduce the production of cortisol. Pharmacological options remain very limited and there is an unmet medical need for additional medicines, especially when surgery fails or for patients who cannot undergo surgery or take other medicines.

A medicine used off-label for more than 30 years

Doctors have used ketoconazole to treat Cushing's syndrome for more than 30 years, although it has never been authorised for this indication in the EU. The CHMP's recommendation builds on information from published literature and documented use in clinical practice where this medicine was used "off-label", that is, outside its authorised indications.

Ketoconazole-containing medicines have been authorised in a number of EU countries to treat fungal infections. However, in July 2013, the CHMP recommended to suspend the marketing authorisations of these medicines when used by mouth. Following an EU-wide review, the CHMP concluded that when ketoconazole was given by mouth to treat fungal infections, the risk of liver injury was greater than its benefits, specifically in view of available alternative treatments, which are considered safer. This

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suspension did not include ketoconazole applied to the skin, which is still approved for use in many EU countries.

When assessing Ketoconazole HRA for the treatment of Cushing's syndrome, the CHMP considered that in this rare and potentially life-threatening condition, the medicine's benefits are greater than its risks, which can be manageable in clinical practice by specific measures mitigating the risk of liver toxicity including close monitoring of the patients' liver function. Ketoconazole HRA is to be prescribed only by physicians specalised in treating Cushing's syndrome as the posology needs to be individualised for each patient. Information will be sent to healthcare professionals to allow them to advise patients and prescribe the medicine safely and effectively.

At the time of the suspension of ketoconazole for fungal infections, healthcare professionals and patients were concerned that ketoconazole would no longer be available for patients with Cushing's syndrome. The CHMP reviewed Ketoconazole HRA through accelerated assessment, to facilitate patients' access to a fully authorised medicine as soon as possible with evidence-based information for patients and doctors.

The opinion adopted by the CHMP at its September 2014 meeting is an intermediary step on Ketoconazole HRA's path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will then take place at the level of each Member State considering the potential role/use of this medicine in the context of the national health system of that country.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. The marketing-authorisation applicant for Ketoconazole HRA is Laboratoire HRA Pharma.
3. More information on the review concluded in July 2013 by the EMA for oral ketoconazole-containing medicines in the treatment of fungal infections is available here.
4. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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