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Questions and answers

Withdrawal of the marketing authorisation application for Ketoconazole AID-SCFM (ketoconazole)

On 23 February 2015, Agenzia Industrie Difesa - Stabilimento Chimico Farmaceutico Militare officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Ketoconazole AID-SCFM, for the treatment of Cushing's syndrome.

What is Ketoconazole AID-SCFM?

Ketoconazole AID-SCFM is a medicine that contains the active substance ketoconazole. It was to be available as 200 mg capsules.

What was Ketoconazole AID-SCFM expected to be used for?

Ketoconazole AID-SCFM was expected to be used to treat adults with Cushing's syndrome for whom surgery was not an option or had failed. Cushing's syndrome is a disease characterised by an excess production of the hormone cortisol by the adrenal glands, two glands situated above the kidneys.

Ketoconazole AID-SCFM was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 9 August 2012 for Cushing's syndrome.

How is Ketoconazole AID-SCFM expected to work?

The active substance in Ketoconazole AID-SCFM, ketoconazole, blocks the activity of a group of enzymes involved in the production of cortisol by the adrenal glands, such as 17 alpha-hydroxylase or 11b-hydroxylase. Blocking cortisol production will help to reduce cortisol levels in the body, thereby relieving the symptoms of the disease. Ketoconazole can also block the production of other hormones produced by the adrenal gland which are often raised in Cushing's syndrome.

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Another medicine containing ketoconazole (Ketoconazole HRA) was recently approved in the EU to treat Cushing's syndrome.

What did the company present to support its application?

Because ketoconazole is a well-known substance and its use in Cushing's syndrome is well established, the applicant presented data from the published literature to support its application for Ketoconazole AID-SCFM.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the initial documentation provided by the company and formulated a list of questions. The company had not yet responded to the questions at the time of the withdrawal.

What was the recommendation of the CHMP at that time?

Based on the initial review of the data, at the time of the withdrawal, the CHMP had several concerns and was of the provisional opinion that Ketoconazole AID-SCFM could not have been approved for the treatment of Cushing's syndrome. The Committee had concerns over the quality of the medicine (in particular on the choice of the starting material to make the medicine and the presence of impurities). In addition, the CHMP had concerns about the documentation submitted in support of the effectiveness and safety of the medicine.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Ketoconazole AID-SCFM did not outweigh its risks.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of application, the applicant stated that it was withdrawing the application since it would require a further time extension to provide the responses to the CHMP's questions. The company also cited commercial reasons, since another medicine containing ketoconazole for Cushing's syndrome was recently authorised in the EU.

The withdrawal letter is available here.

The summary of the opinion of the Committee for Orphan Medicinal Products for Ketoconazole AID-SCFM can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.