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Questions and answers

Withdrawal of the marketing authorisation application for Loulla (mercaptopurine)

On 19 December 2012, Only For Children Pharmaceuticals officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Loulla, for the maintenance treatment of acute lymphoblastic leukaemia.

What is Loulla?

Loulla is a medicine that contains the active substance mercaptopurine. It was to be available as tablets and a solution to be made up into an suspension to be taken by mouth (10 mg/ml).

What was Loulla expected to be used for?

Loulla was expected to be used for the maintenance treatment of patients with acute lymphoblastic leukaemia (ALL), a cancer of the lymphocytes (a type of white blood cell).

Loulla was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 22 October 2007 for ALL.

How is Loulla expected to work?

The active substance in this medicine, mercaptopurine, has a similar chemical structure to purines, which are one of the fundamental chemicals that make up DNA. In the body, mercaptopurine is converted within cells into a substance that interferes with the production of new DNA. This prevents the cells from dividing. In ALL, the lymphocytes multiply too quickly and live for too long. Mercaptopurine prevents the lymphocytes from dividing and they eventually die, thereby slowing down the progression of the leukaemia.

Medicines containing mercaptopurine in tablet form have already been used in the European Union (EU) for many years to treat patients with ALL. Xaluprine, which contains mercaptopurine in an oral suspension, was authorised in the EU for ALL on 9 March 2012.

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What did the company present to support its application?

Because it is an orphan medicine, Xaluprine was granted a 10-year market exclusivity at the time of its authorisation in March 2012. The market exclusivity prevents similar medicines from being authorised for the same condition until March 2022.

As the CHMP considered Loulla to be a similar medicine to Xaluprine, the company for Loulla applied for a legal exemption that could have allowed Loulla to be authorised in spite of Xaluprine's market exclusivity based on its clinical superiority. The company's application for exemption was based on the claim that Loulla is more palatable than Xaluprine and that its other ingredients called excipients are safer to use. The company also claimed that it is safer to administer with a lower risk of spillage and accidental overdosage due to the design of the container. The company presented its case for the clinical superiority of Loulla, which included results of a small clinical study in children and young adults.

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

The application was withdrawn after the CHMP had evaluated the report 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 review of the report, the CHMP had some concerns and was of the provisional opinion that Loulla was not clinically superior to Xaluprine and could not have been approved for the treatment of ALL.

The CHMP was of the view that there was no good evidence that Loulla would offer patients any important advantages over Xaluprine. Although the CHMP agreed that Loulla was shown to be palatable for children, the Committee did not agree that there was any evidence to suggest that the composition of Loulla or the design of its container made Loulla safer to use or administer than Xaluprine.

In addition, a routine inspection performed at three clinical study sites revealed that the study was not conducted in full compliance with Good Clinical Practice (GCP) and cast doubt on the reliability of the results from one of the sites.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the company had not shown clinical superiority of Loulla over Xaluprine.

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

In its letter notifying the Agency of the withdrawal of application, the company stated that it decided to withdraw the application since the CHMP considered that there was insufficient evidence to show that Loulla was clinically superior to Xaluprine.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate use programmes using Loulla.

If you are in a clinical trial or compassionate use programme and need more information about your treatment, contact the doctor who is giving it to you.

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