29 June 2018
EMA/431413/2018
EMEA/H/C/004736

Withdrawal of the marketing authorisation application for Graspa (L-asparaginase)

On 22 June 2018, Erytech Pharma S.A. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Graspa, for the treatment of acute lymphoblastic leukaemia (ALL).

What is Graspa?

Graspa is a cancer medicine that contains the active substance L-asparaginase that has been enclosed in red blood cells. Asparaginase has been used to treat cancer for many years and is authorised in EU countries under several trade names. Graspa was intended to be given by infusion (drip) into a vein.

What was Graspa expected to be used for?

Graspa was expected to be used in combination with other cancer medicines to treat adults and children with ALL that was not related to a particular genetic change (known as 'Philadelphia chromosome negative'). It was to be used if the ALL did not improve with standard treatment or if it had come back after such treatment.

Graspa was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 27 October 2006 for ALL. Further information on the orphan designation can be found here.

How does Graspa work?

Asparagine is an amino acid produced by healthy cells in the body. However, lymphoblastic leukaemia cells cannot produce the amino acid and therefore they take it from the blood since they need it for their rapid growth. Giving the enzyme L-asparaginase destroys asparagine in the blood and deprives the leukaemia cells of this amino acid, causing them to die.

In Graspa, L-asparaginase is enclosed in red blood cells because it was expected that this would allow the enzyme to work while protecting it from being broken down in blood and from antibodies that may attach to it and stop it from working.

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What did the company present to support its application?

The company provided data from a main study which compared Graspa with asparaginase (not enclosed in blood cells) in 80 patients aged 1 to 55 years with Philadelphia chromosome negative ALL whose disease had not improved with other treatment or had come back.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the initial documentation provided by the company and formulated a list of questions.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 review of the data, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Graspa could not have been approved for the treatment of ALL. The CHMP was concerned that the medicine contains a different type of asparaginase to that used in clinical studies and that the data provided were not sufficient to show how the medicine behaved in the body or how well it worked compared with other asparaginase medicines. Also, data were too limited to show how much Graspa's effectiveness was reduced by antibodies or how safe it was in children or after repeated treatments.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that, because of lack of proven effectiveness, the benefits of Graspa 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 the application, the company stated that the data provided were not sufficient to conclude on Graspa's benefit and risk.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials using Graspa.

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