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Questions and answers

Withdrawal of the marketing authorisation application for Cerepro (sitimagene ceradenovec)

On 8 March 2010, Ark Therapeutics officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Cerepro, which was intended to be used with ganciclovir sodium to treat operable high grade glioma.

What is Cerepro?

Cerepro is a concentrate for solution for injection that contains the active substance sitimagene ceradenovec.

Cerepro was developed as a type of advanced therapy medicine called a 'gene therapy product'. This is a type of medicine that works by delivering genes into the body.

What was Cerepro expected to be used for?

Cerepro was to be used in combination with a medicine called ganciclovir sodium to treat high-grade glioma in patients who are eligible for surgery. Glioma is a type of brain tumour that begins in 'glial' cells (the cells that surround and support nerve cells).

Cerepro was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 6 February 2002 for high grade glioma.

How was Cerepro expected to work?

The active substance in Cerepro, sitimagene ceradenovec, is a type of virus that has been modified so it can carry a gene for the protein 'thymidine kinase' into the body. The virus in Cerepro is an 'adenovirus' that has been engineered so that it cannot make copies of itself and therefore does not cause infections in humans.

When Cerepro is injected into the brain at the time of surgery, the modified virus is taken up by the cells near the injection sites. The cells then start to produce the thymidine kinase. This protein was

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expected to work by helping to convert the medicine ganciclovir sodium into a form which can kill cells that are dividing. The cells to be killed by ganciclovir sodium were mainly these rapidly dividing cancer cells. Normal nerve cells and cells outside the tumour were expected to be less affected.

What did the company present to support its application?

The effects of Cerepro were first tested in experimental models before being studied in humans. The company also presented data from one main study involving 251 patients with glioma that could be operated on. The study compared the effects of adding Cerepro and ganciclovir sodium to standard treatment with the effects of standard treatment alone. The main measure of effectiveness was how long the patients lived without the need for additional treatments to prolong their lives. The study also looked at how long the patients survived.

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

The evaluation had finished and the CHMP had given a negative opinion. The company had requested a re-examination of the negative opinion, but this re-examination had not yet finished when the company withdrew.

What was the recommendation of the CHMP at that time?

Because Cerepro is an advanced therapy medicine, it was assessed by the Committee for Advanced Therapies (CAT). Taking into account the assessment performed by the CAT, the CHMP concluded that, based on the results of the main study, including the main measure of effectiveness, Cerepro was not shown to be effective. Finally, Cerepro was associated with an increased risk of serious side effects such as hemiparesis (paralysis on one side of the body) and seizures (fits). These side effects were a concern, considering the lack of proven effectiveness.

At that point in time, because of lack of proven effectiveness, the CHMP was of the opinion that the benefits of Cerepro did not outweigh its risks and recommended that it be refused marketing authorisation.

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

The letter from the company notifying the Agency of the withdrawal of the application is available here.

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

The company informed the CHMP that, at the time of the withdrawal, there were no clinical trials or formal compassionate use programmes with Cerepro.

The summary of the opinion of the Committee for Orphan Medicinal Products for Cerepro is available here.