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Questions and answers on the recommendation for the refusal of the marketing authorisation for Cerepro (sitimagene ceradenovec)

On 17 December 2009, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Cerepro, intended for use with ganciclovir sodium for the treatment of operable high grade glioma.

The company that applied for authorisation is Ark Therapeutics. It may request a re examination of the opinion within 15 days of receipt of notification of this negative opinion.

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. The new genes then make the body produce or stop the production of a protein which may help treat a disease.

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 enzyme (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.

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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 enzyme. This enzyme was expected to work by helping to convert the medicine ganciclovir sodium into a form which can kill cells that are dividing, including any cancerous cells that were not removed during the operation.

What documentation did the company present to support its application to the Agency?

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.

What were the major concerns that led the CHMP to recommend the refusal of the marketing authorisation?

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 the results of the main study did not show that Cerepro was effective. In addition, Cerepro was associated with an increased risk of serious side effects such as hemiparesis (slight 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, 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 are the consequences of the refusal for patients in clinical trials or compassionate use programmes using Cerepro?

The company informed the CHMP that there are currently no clinical studies or formal compassionate use programmes with Cerepro. The company will make the medicine available for named patient use, which is when a doctor makes a request for a medicine to treat a patient before the medicine is licensed.

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