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Questions and answers on the withdrawal of the marketing authorisation application for Contusugene Ladenovec Gendux

contusugene ladenovec

On 12 June 2009, Gendux Molecular Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Contusugene Ladenovec Gendux for the treatment of recurrent or refractory squamous cell carcinoma of the head and neck.

What is Contusugene Ladenovec Gendux?
Contusugene Ladenovec Gendux is a suspension for injection that contains the active substance contusugene ladenovec.
Contusugene Ladenovec Gendux 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 Contusugene Ladenovec Gendux expected to be used for?
Contusugene Ladenovec Gendux was expected to be used to treat squamous cell carcinoma of the head and neck (a type of cancer that starts in the cells lining the mouth, nose, throat or ear). It was to be used when the cancer was refractory (does not respond to treatment) or recurrent (keeps coming back).

How is Contusugene Ladenovec Gendux expected to work?
The active substance in Contusugene Ladenovec Gendux, contusugene ladenovec, is a type of virus that has been modified so that it can carry the p53 gene into the cells of the body.
Once injected into the tumour, Contusugene Ladenovec Gendux was expected to carry the p53 gene into the cancer cells, where the gene was expected to make the cell increase the production of the p53 protein. The p53 protein normally contributes to the repair of damaged DNA, causes cell death when the DNA cannot be repaired and helps control the formation of blood vessels. Because cancer cells contain damaged DNA, the p53 protein either helps to repair the DNA or causes the cells to die. The p53 protein also reduces the formation of blood vessels supplying the cancer cells.
By increasing the production of the p53 protein, Contusugene Ladenovec Gendux was expected to cure or slow down the growth of the cancer.
The virus in Contusugene Ladenovec Gendux is an 'adenovirus' that has been modified so that it does not cause disease in humans.

What documentation did the company present to support its application to the CHMP?
The effects of Contusugene Ladenovec Gendux were first tested in experimental models before being studied in humans. In one main study involving 123 patients with refractory or recurrent squamous cell carcinoma of the head and neck, Contusugene Ladenovec Gendux was compared with methotrexate (another anti-cancer medicine). The main measure of effectiveness was how long the patients lived.

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How far into the evaluation was the application when it was withdrawn?
The application was at day 120 of the procedure when the company withdrew. In 2008, the CHMP had formulated a list of questions to be answered by the company. The company had to submit their responses to the Committee for Advanced Therapies (CAT) in line with new European Union regulations on advanced therapies. But, the company withdrew its application before responding to the questions.

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 Contusugene Ladenovec Gendux could not have been approved for the treatment of recurrent or refractory squamous cell carcinoma of the head and neck.

What were the main concerns of the CHMP?
The Committee was of the opinion that the company had not shown that Contusugene Ladenovec Gendux was beneficial to patients. Also, the company had not supplied enough evidence to demonstrate that the product was safe, that it could be made in a reliable manner, or that it would not be harmful to the environment or to people in close contact with the patient.
Finally, the CHMP noted that there was insufficient information on the product's toxicity, its distribution in the body and the role of some genes and impurities found in the product.

What were the reasons given by the company for withdrawing the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients in clinical trials or compassionate use programmes using Contusugene Ladenovec Gendux?
The Company did not inform the Agency of any patients in clinical trials or compassionate use programmes using Contusugene Ladenovec Gendux.