European Medicines Agency

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QUESTIONS AND ANSWERS ON RECOMMENDATION FOR THE REFUSAL OF THE MARKETING AUTHORISATION
for
GENASENSE

International non-proprietary name (INN): ***oblimersen***

On 26 April 2007, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Genasense 30 mg/ml concentrate for solution for infusion, intended for the treatment of advanced or metastatic melanoma. The company that applied for authorisation is Genta Development Limited. The applicant requested a re-examination of the opinion. After having considered the grounds for this request, the CHMP re-examined the initial opinion, and confirmed the refusal of the marketing authorisation on 19 July 2007.

What is Genasense?
Genasense is a medicine containing the active substance oblimersen. It is made up into a solution that is given as an intravenous infusion (drip into a vein).

What was Genasense expected to be used for?
Genasense was to be used to treat patients with melanoma (a type of skin cancer affecting cells called 'melanocytes') whose disease is advanced (it cannot be removed by surgery alone) or metastatic (has spread to other parts of the body). Genasense was to be used in combination with dacarbazine (another anticancer medicine).

How is Genasense expected to work?
The active substance in Genasense, oblimersen, is an antineoplastic medicine. It is thought to work by preventing cells from producing the protein Bcl-2. This protein normally allows skin cancer cells to stay alive by preventing them from committing suicide (apoptosis). By blocking the production of Bcl-2, Genasense was expected to make the cancer cells more sensitive to factors that cause cell death, including anticancer medicines such as dacarbazine. This was expected to slow down the growth of the tumour.
Oblimersen is an 'anti-sense oligonucleotide' medicine. It attaches to the 'messenger RNA' (mRNA) that normally instructs the cell how to make Bcl-2. This stimulates the cell to destroy the mRNA, blocking the production of the protein.

What documentation did the company present to support its application to the CHMP?
The effects of Genasense were first tested in experimental models before being studied in humans. Genasense has also been studied in 771 patients with advanced or metastatic melanoma. The effects of Genasense in combination with dacarbazine were compared with those of dacarbazine taken alone. The main measure of effectiveness was survival.

What were the major concerns that led the CHMP to recommend the refusal of the marketing authorisation?
In the main study of patients with melanoma, survival rates were very similar in the patients receiving Genasense with dacarbazine and those receiving dacarbazine alone. Therefore, the study did not

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demonstrate that Genasense was effective in treating melanoma. There were side effects associated with treatment with Genasense.
At that point in time, the CHMP was of the opinion that the benefits of Genasense in the treatment of advanced or metastatic melanoma did not outweigh its risks. Hence, the CHMP recommended that Genasense be refused marketing authorisation. The CHMP refusal was confirmed after re-examination.

What are the consequences of the refusal for patients in clinical trials or compassionate use programmes using Genasense?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate use programmes with Genasense. 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.