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Questions and answers

Withdrawal of the marketing authorisation application for Jenzyl (ridaforolimus)

On 27 November 2012, Merck Sharp & Dohme Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Jenzyl, for the maintenance treatment of patients with metastatic soft tissue sarcoma or bone sarcoma previously treated with chemotherapy.

What is Jenzyl?

Jenzyl is a medicine that contains the active substance ridaforolimus. It was to be available as 10 mg tablets.

What was Jenzyl expected to be used for?

Jenzyl was expected to be used for the treatment of adults with soft tissue sarcoma (a type of cancer that affects the soft, supporting tissues of the body) or bone sarcoma (bone cancer) that are metastatic (have spread to other parts of the body).

It was expected to be used as maintenance therapy in patients who have already received two or three regimens of chemotherapy.

Jenzyl was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 26 August 2005 and 28 October 2005 for the treatment of soft tissue sarcoma and primary malignant bone tumours.

How is Jenzyl expected to work?

The active substance in Jenzyl, ridaforolimus, blocks the action of an enzyme called 'mammalian target of rapamycin' (mTOR), which regulates the growth and division of cells in the body and which has increased activity in patients with sarcoma. In the body, ridaforolimus first attaches to a protein called FKBP-12 that is found inside cells to make a 'complex'. This complex then blocks mTOR. Since mTOR is

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involved in the control of cell division and the growth of blood vessels, ridaforolimus prevents the division of tumour cells and reduces their blood supply. This is expected to slow down the growth and proliferation of cancer cells.

What did the company present to support its application?

The company presented the results of one main study involving 711 patients with metastatic soft tissue sarcoma or bone sarcoma who have received up to four cycles of one, two or three alternative chemotherapy regimens. The study compared Jenzyl with placebo (a dummy treatment). The main measure of effectiveness was the time patients lived until their disease got worse.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated a list of questions. The company had not yet responded to the last round of questions at the time of the withdrawal.

What was the recommendation of the CHMP at that time?

Based on the review of the data and the company's response to the CHMP list of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Jenzyl could not have been approved for the treatment of patients with metastatic soft tissue sarcoma or bone sarcoma as maintenance therapy.

The CHMP was concerned that taking Jenzyl only led to a small increase in the time patients lived until their disease got worse compared with placebo (18 versus 15 weeks in patients who had one or more regimens of previous chemotherapy, and 16 versus 10 weeks in patients who had received two or three previous regimens of chemotherapy). The CHMP considered this benefit to be modest, when taking into account that patients usually survived for a long time after their disease had progressed. The CHMP also considered that the somewhat larger effect seen in patients who had received two or three previous regimens of chemotherapy compared with those who received one or more regimens might not reflect the medicine's true effect size, as the reason the medicine would work better at later stages of the disease was unclear. In terms of safety, the CHMP was concerned by the high frequency of side effects interfering with the patient's wellbeing as well as some uncommon but potentially life-threatening side effects.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Jenzyl 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 application, the company stated that it decided to withdraw the application since the CHMP considered that the data provided did not allow the Committee to conclude on a positive benefit-risk balance.

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 Jenzyl.

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

The summary of the opinion of the Committee for Orphan Medicinal Products for Jenzyl can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation (soft tissue sarcoma and primary malignant bone tumours).