European Medicines Agency

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Questions and answers on recommendation for the refusal of the marketing authorisation for Ixempra

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

On 20 November 2008, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Ixempra 2 mg/ml powder and solvent for concentrate for solution for infusion, intended for the treatment of locally advanced or metastatic breast cancer. The company that applied for authorisation is Bristol-Myers Squibb Pharma EEIG. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Ixempra?
Ixempra is a medicine that contains the active substance ixabepilone. It was to be available as a powder and a solvent to be made up into a solution for infusion (drip into a vein).

What was Ixempra expected to be used for?
Ixempra was expected to be used to treat breast cancer that is locally advanced or metastatic (when the tumour is large or has begun to spread within the body). It was to be used when previous treatment with cytotoxic medicines (medicines that kill cells that are dividing, such as cancer cells) had failed, either in combination with capecitabine (another anticancer medicine) or on its own.

How is Ixempra expected to work?
The active substance in Ixempra, ixabepilone, is a cytotoxic medicine that belongs to a new group of medicines called the 'epothilones'. Ixabepilone is expected to block the ability of cells to modify the internal 'skeleton' that they need to divide and multiply. With the skeleton unable to change, the cancer cells cannot divide and they eventually die. Ixabepilone is also expected to affect non-cancer cells such as nerve cells, which could cause side effects.

What documentation did the company present to support its application to the CHMP?
The effects of Ixempra were first tested in experimental models before being studied in humans.
Ixempra has been studied in three main studies involving women with locally advanced or metastatic breast cancer who had been treated with a number of other anticancer medicines in the past.
The first study looked at Ixempra given on its own in 128 women, but did not compare it with any other treatment. The main measure of effectiveness was the number of patients whose cancer responded to treatment.
The other two studies compared the effects of capecitabine given on its own with the effects of Ixempra given in combination with capecitabine in a total of 1,973 women. The main measures of effectiveness were the length of time before the patient's cancer started to get worse and how long the patients survived.

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

The CHMP was concerned that the Ixempra's benefits in terms of increasing the time until the cancer got worse and the very small increase in survival did not outweigh the concerns over the medicine's safety. In particular, the Committee was concerned over neuropathy (damage to nerve cells), which was a severe and common side effect in patients taking the medicine.

At that point in time, the CHMP was of the opinion that the benefits of Ixempra in the treatment of breast cancer did not outweigh its risks. Hence, the CHMP recommended that Ixempra be refused marketing authorisation.

What are the consequences of the refusal for patients in clinical trials or compassionate use programmes using Ixempra?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials or compassionate use programmes with Ixempra. 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.