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Questions and answers

Withdrawal of the marketing authorisation application for Doxorubicin SUN (doxorubicin)

On 20 Jul 2011, Sun Pharmaceutical Industries Europe B.V. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Doxorubicin SUN, intended for the treatment of metastatic breast cancer, advanced ovarian cancer and progressive multiple myeloma.

What is Doxorubicin SUN?

Doxorubicin SUN is concentrate to be made up into a solution for infusion (drip into a vein). It contains the active substance doxorubicin (2 mg/ml).

Doxorubicin SUN was assessed as a 'hybrid generic medicine'. This means that it is similar to a 'reference medicine' already authorised in the European Union containing the same active substance, called Caelyx.

What was Doxorubicin SUN expected to be used for?

Doxorubicin SUN was expected to be used to treat the following types of cancer in adults:

- metastatic breast cancer in patients at risk of heart problems. 'Metastatic' means the cancer has spread to other parts of the body. Doxorubicin SUN was expected to be used on its own for this disease;
- advanced ovarian cancer (cancer of the ovary) in women whose previous treatment including a platinum-based anticancer medicine has stopped working;
- multiple myeloma (a cancer of the cells in the bone marrow), in patients with progressive disease who have received at least one other treatment in the past and have already undergone or are

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unsuitable for a bone marrow transplant. Doxorubicin SUN was to be used in combination with bortezomib (another anticancer medicine).

Doxorubicin SUN was originally also expected to be used to treat AIDS-related Kaposi's sarcoma (a cancer of the blood vessels) but this indication was withdrawn during the evaluation process.

How was Doxorubicin SUN expected to work?

Doxorubicin SUN was expected to work in the same way as the reference medicine, Caelyx. The active substance in Doxorubicin SUN and Caelyx, doxorubicin, is a cytotoxic medicine that belongs to the group 'anthracyclines'. It works by interfering with the DNA within cells, preventing them from making more copies of DNA and making proteins. This means that cancer cells cannot divide and eventually die. Doxorubicin accumulates in areas of the body where the blood vessels have an abnormal shape, such as within tumours, where its action is concentrated.

In Caelyx and Doxorubicin SUN, doxorubicin is contained (encapsulated) in 'pegylated liposomes' (tiny fatty spheres that are coated with a chemical called polyethylene glycol). This reduces the rate at which the active substance is broken down, allowing it to circulate in the blood for longer. It also reduces its effects on non-cancer tissues and cells, so it is less likely to cause some side effects. The active substance has an effect in the body when it is released (freed) from the liposome.

What did the company present to support its application?

Because Doxorubicin SUN was assessed as a hybrid generic medicine, the company presented the results of studies carried out to investigate whether it is similar to the reference medicine. These included studies in patients with ovarian cancer and multiple myeloma to investigate the concentrations of doxorubicin in the blood produced by Doxorubicin SUN compared with Caelyx. This included the total amount of doxorubicin and the amounts of liposome-encapsulated doxorubicin, free doxorubicin and doxorubicinol (the main metabolite of doxorubicin). The company also presented the results of animal studies showing the distribution of the two medicines in different body tissues such as the heart, skin, kidney and spleen, since this could not be studied in humans.

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

The application was withdrawn after 'day 181'. This means that the CHMP had evaluated the documentation provided by the company and formulated a list of questions. After the CHMP had assessed the company's responses to the last round of questions, there were still some unresolved issues.

What was the recommendation of the CHMP at that time?

Based on the review of the data and the company's responses to the CHMP lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Doxorubicin SUN could not have been approved. Based on the data submitted, the CHMP was of the opinion that the studies did not provide enough evidence to show that Doxorubicin SUN was similar to the reference medicine. Therefore, at the time of the withdrawal, the CHMP was of the opinion that the company had not provided enough data to support the application for Doxorubicin SUN.

What were the reasons given by the company for withdrawing the application?

The letter from the company notifying the Agency of the withdrawal of the application is available under the tab ‘All documents’.