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Withdrawal of application for the marketing authorisation of Doxorubicin hydrochloride Tillomed (doxorubicin hydrochloride pegylated liposomal concentrate for dispersion for infusion, 2 mg/ml)

Laboratorios Tillomed Spain S.L.U. withdrew its application for a marketing authorisation of Doxorubicin Hydrochloride Tillomed for the treatment of breast and ovarian cancer, multiple myeloma and AIDS-related Kaposi's sarcoma.

The company withdrew the application on 2 March 2020.

What is Doxorubicin hydrochloride Tillomed and what was it intended to be used for?

Doxorubicin hydrochloride Tillomed was developed as a medicine to be used for the treatment of breast and ovarian cancer, multiple myeloma and AIDS-related Kaposi's sarcoma.

Doxorubicin hydrochloride Tillomed contains the active substance doxorubicin, a well-known cancer medicine that has been used in the EU for many years, and was to be available as a concentrate for making up an infusion.

Doxorubicin hydrochloride Tillomed was developed as a hybrid 'medicine'. This means that it was intended to be similar to a 'reference medicine' already authorised in the European Union called Adriamycin. The difference between the products is that in Doxorubicin hydrochloride Tillomed the active substance doxorubicin is enclosed in tiny fatty spheres called liposomes.

Doxorubicin hydrochloride Tillomed was also developed as a generic medicine. This means that it contained the same active substance as an authorised 'reference medicine' Caelyx and was intended to work in the same way.

For more information on generic medicines, see the question-and-answer document here.

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How does Doxorubicin hydrochloride Tillomed work?

The active substance in Doxorubicin hydrochloride Tillomed, Adriamycin and Caelyx, doxorubicin, is a cytotoxic substance 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. The medicine builds up in areas in the body where the blood vessels have an abnormal shape, such as within tumours, where its action is concentrated.

As in Caelyx, the doxorubicin in Doxorubicin hydrochloride Tillomed is contained 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 effects on non-cancer tissues and cells, so the medicine is less likely to cause some side effects.

What did the company present to support its application?

Studies on the benefits and risks of the active substance are not needed for a generic medicine because they have already been carried out with the reference medicine. As for every medicine, the company provided studies on the quality of Doxorubicin hydrochloride Tillomed. It also provided studies to investigate whether Doxorubicin hydrochloride Tillomed is 'bioequivalent' to the comparator medicine Caelyx. Two medicines are bioequivalent when they produce the same levels of the active substance in the body and are therefore expected to have the same effect.

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

The application was withdrawn after the European Medicines Agency had evaluated the information from the company and prepared questions for the company. The company had not responded to the last round of questions at the time of the withdrawal.

What did the Agency recommend at that time?

Based on the review of the data and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Doxorubicin hydrochloride Tillomed could not have been authorised for the requested indications.

In particular, although the results of the bioequivalence study suggested that Doxorubicin hydrochloride Tillomed was comparable to Caelyx, the Agency had concerns about these findings following an inspection of one of the clinical sites where the study had been carried out and of the site where the data analysis took place.

The inspections found some serious deficiencies in following Good Clinical Practice (GCP), notably the way the results had been documented, and raised concerns about how they had been analysed. Therefore, at the time of the withdrawal, the Agency's opinion was that the results of the study were not reliable and it concluded that the medicine could not have been authorised based on the data from the company.

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

In its letter notifying the Agency of the withdrawal of the application, the company stated that it was withdrawing its application because of the identified deficiencies in Good Clinical Practice at the test site.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials using Doxorubicin hydrochloride Tillomed.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.