European Medicines Agency

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QUESTIONS AND ANSWERS ON RECOMMENDATION FOR THE REFUSAL OF A CHANGE TO THE MARKETING AUTHORISATION
for
Taxotere/Docetaxel Winthrop

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

On 24 July 2008, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of a change to the marketing authorisation for the medicinal product Taxotere/Docetaxel Winthrop concentrate and solvent for solution for infusion. The change concerned an extension of indication to add the treatment of patients with operable breast cancer whose tumours overexpress HER2 in combination with trastuzumab, with or without carboplatin. The company that applied for authorisation is Aventis Pharma S.A. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Taxotere/Docetaxel Winthrop?
Taxotere/Docetaxel Winthrop is a concentrate and solvent, which are made up into a solution for infusion (drip into a vein). It contains the active substance docetaxel.
Taxotere/Docetaxel Winthrop is an anticancer medicine. It is used in breast cancer that is advanced or 'metastatic' (has spread to other parts of the body), and in breast cancer that can be treated with surgery. In these patients, Taxotere/Docetaxel Winthrop is used in addition to surgery to remove the tumour, together with doxorubicin and cyclophosphamide (other anticancer medicines).
Taxotere/Docetaxel Winthrop is also used in advanced or metastatic non-small cell lung cancer, in prostate cancer, in metastatic gastric adenocarcinoma (a type of stomach cancer) and in advanced head and neck cancer.

What was Taxotere/Docetaxel Winthrop expected to be used for?
Taxotere/Docetaxel Winthrop was also expected to be used to treat breast cancer that can be treated with surgery when the cancer has been shown to be 'expressing' large amounts of HER2: this is a type of cancer that produces (expresses) a specific protein called HER2 in large quantities on the surface of the tumour cells.
Taxotere/Docetaxel Winthrop was expected to be used in addition to surgery to remove the tumour in the following treatment combinations:
- in combination with trastuzumab (another anticancer medicine), following treatment with doxorubicin and cyclophosphamide;
- in combination with trastuzumab and carboplatin (another anticancer medicine).

How is Taxotere/Docetaxel Winthrop expected to work?
The active substance in Taxotere/Docetaxel Winthrop, docetaxel, belongs to the group of anticancer medicines known as the 'taxanes'. Docetaxel blocks the ability of cells to destroy the internal 'skeleton' that allows them to divide and multiply. With the skeleton still in place, the cells cannot divide and they eventually die. Docetaxel affects not only cancer cells, but also non-cancer cells such as blood cells, which can cause side effects.

What documentation did the company present to support its application to the CHMP?
Taxotere/Docetaxel Winthrop has been studied in one main study involving over 3,000 women with HER2-expressing breast cancer that could be treated with surgery. The study compared the effectiveness of the following treatment combinations, which were used in addition to surgery:

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- the combination of doxorubicin and cyclophosphamide for 12 weeks, followed by Taxotere/Docetaxel Winthrop for 12 weeks, either alone or in combination with trastuzumab;
- the combination of Taxotere/Docetaxel Winthrop, trastuzumab and carboplatin for 18 weeks.

In both groups, trastuzumab treatment was continued for a year. The main measure of effectiveness was how long the patients survived until their cancer came back.

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

The CHMP was concerned that it was not possible to establish the benefits of the treatment combinations including Taxotere/Docetaxel Winthrop when used in addition to surgery, because of the way the single main study was designed. The CHMP was also concerned that the company did not provide sufficient clinical evidence to justify the use of the combination of Taxotere/Docetaxel Winthrop, carboplatin and trastuzumab.

Therefore, at that point in time, the CHMP was of the opinion that the benefits of Taxotere/Docetaxel Winthrop in the treatment of patients with operable breast cancer whose tumours overexpress HER2 in combination with trastuzumab, with or without carboplatin, did not outweigh its risks. Hence, the CHMP recommended that the change to the marketing authorisation be refused.

What are the consequences of the refusal for patients in clinical trials using Taxotere/Docetaxel Winthrop?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Taxotere/ Docetaxel Winthrop. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening for Taxotere/Docetaxel Winthrop for the treatment of other types of breast cancer, non-small cell lung cancer, prostate cancer, gastric adenocarcinoma and head and neck cancer?

There are no consequences on the use of Taxotere/Docetaxel Winthrop in its authorised indications, for which the balance of benefits and risks remains unchanged.