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EPAR summary for the public

Herceptin

trastuzumab

This document is a summary of the European public assessment report (EPAR) for Herceptin. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Herceptin.

What is Herceptin?

Herceptin is a medicine that contains the active substance trastuzumab. It is available as a powder to be made up into a solution for infusion (drip) into a vein or as a solution for injection under the skin.

What is Herceptin used for?

Herceptin is used to treat the following types of cancer:

- early breast cancer (when the cancer has spread within the breast or to the glands under the arm but not to other parts of the body) after surgery, chemotherapy (medicines to treat cancer), and radiotherapy (treatment with radiation) if applicable. It can also be used earlier in treatment, in combination with chemotherapy. For tumours that are locally advanced (including those that are inflammatory) or more than 2 cm wide, Herceptin is used before surgery in combination with chemotherapy and then again after surgery on its own;
- metastatic breast cancer (cancer that has spread to other parts of the body). It is used on its own in patients in whom previous treatments have failed. It is also used in combination with other anticancer medicines: with paclitaxel or docetaxel, or with an aromatase inhibitor;

When used as an infusion into a vein, Herceptin can also be used for:

- metastatic gastric (stomach) cancer, in combination with cisplatin and either capecitabine or 5-fluorouracil (other anticancer medicines).

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Herceptin can only be used when the cancer has been shown to 'overexpress HER2': this means that the cancer produces a protein called HER2 in large quantities on the surface of the tumour cells, which makes the tumour cells grow more quickly. HER2 is overexpressed in about a quarter of breast cancers and a fifth of gastric cancers.

The medicine can only be obtained with a prescription.

How is Herceptin used?

Herceptin treatment should only be started by a doctor who has experience in the use of anticancer medicines.

When given as an infusion into a vein, Herceptin is given over 90 minutes every week or every three weeks for breast cancer, and every three weeks for gastric cancer. For early breast cancer, treatment is given for a year or until the disease comes back, and for metastatic breast or gastric cancer, treatment is continued for as long as it remains effective. The recommended dose depends on the patient's body weight and depends on the condition to be treated and whether Herceptin is given weekly or three-weekly.

The infusion can be associated with allergic reactions, so the patient should be monitored during and after the infusion. Patients who tolerate the first 90-minute infusion can receive subsequent infusions over 30 minutes.

When given as an injection under the skin, the recommended dose of Herceptin does not depend on the patient's body weight and is 600 mg given over 2 to 5 minutes every three weeks.

How does Herceptin work?

The active substance in Herceptin, trastuzumab, is a monoclonal antibody. A monoclonal antibody is an antibody (a type of protein) that has been designed to recognise and attach to a specific structure (called an antigen) that is found on certain cells in the body. Trastuzumab has been designed to attach to HER2, which is overexpressed in about a quarter of breast cancers and a fifth of gastric cancers. By attaching to HER2, trastuzumab activates cells of the immune system, which then kill the tumour cells. Trastuzumab also stops HER2 producing signals that cause the tumour cells to grow.

How has Herceptin been studied?

In early breast cancer, Herceptin given by infusion into a vein has been studied in five main studies involving around 10,000 patients. The first study was in patients who had first been treated with surgery, chemotherapy and radiotherapy (if applicable). Half of the patients received Herceptin, while the other half did not receive it. Three studies looked at the effects of giving Herceptin earlier in treatment, in combination with chemotherapy. A fifth study, in patients with locally advanced or inflammatory breast cancer, looked at the effect of giving Herceptin before surgery in combination chemotherapy and then again after surgery on its own. The studies measured how many patients died or had their cancer reappear or worsen.

In metastatic breast cancer, Herceptin given by infusion into a vein has been studied in four main studies: one looked at Herceptin on its own in 222 patients whose previous treatment had failed; two looked at Herceptin in combination with paclitaxel or docetaxel in a total of 657 patients; and one looked at the combination of Herceptin and anastrozole (an aromatase inhibitor) in 208 women who had been through the menopause. These studies measured how many patients responded to treatment, or how long they lived without their cancer getting worse.

In metastatic gastric cancer, Herceptin given by infusion into a vein in combination with cisplatin and either capecitabine or 5-fluorouracil was compared with the same combination but without Herceptin in one main study involving 594 patients. The main measure of effectiveness was how long the patients survived.

Herceptin given as an injection under the skin was compared with Herceptin given by infusion into a vein in an additional study involving 596 patients with early breast cancer. Herceptin was given before surgery and the main measure of effectiveness was response to treatment assessed by measuring the proportion of patients who had no cancerous cells found on examination of the breast removed by surgery. The study also compared the levels of the active substance in the blood for Herceptin given under the skin and into a vein to demonstrate that sufficient levels are obtained when given under the skin.

All the above studies were in patients whose cancers expressed HER2.

What benefit has Herceptin shown during the studies?

In the first study in early breast cancer, 8% of the patients who received Herceptin by infusion into a vein after having completed surgery, chemotherapy and radiotherapy (if applicable) experienced a reappearance of their cancer in the first year of treatment (127 out of 1,693), compared with 13% of the patients who did not receive it (219 out of 1,693). The addition of Herceptin to chemotherapy resulted in fewer patients experiencing a reappearance of their cancer over three years. The difference was between 4.8 and 11.8% depending on the type of chemotherapy. For locally advanced breast cancer, giving Herceptin by infusion into a vein before surgery in combination with chemotherapy and then again after surgery on its own resulted in fewer patients dying or having their cancer worsen or reappear over three years: after three years, 65% of patients given Herceptin were still alive without having their cancer worsen or reappear as compared to 52% in patients not given Herceptin.

In metastatic breast cancer, 15% of the patients whose previous treatment had failed responded to Herceptin given by infusion into a vein. When used in combination with paclitaxel or docetaxel, around half of the patients responded to Herceptin, compared with around a quarter of those receiving paclitaxel or docetaxel alone. Patients receiving Herceptin in combination with anastrozole also lived for longer without their cancer getting worse (4.8 months, on average) than those receiving anastrozole alone (2.4 months, on average).

In metastatic gastric cancer, the patients with higher levels of HER2 expression who received Herceptin by infusion into a vein survived for an average of 16.0 months, compared with 11.8 months in those receiving cisplatin and either capecitabine or 5-fluorouracil alone.

When given by injection under the skin, Herceptin had the same effectiveness as when given by infusion into a vein. The levels of the active substance were at least as high as when Herceptin is given by infusion into a vein.

What is the risk associated with Herceptin?

The most common or serious side effects with Herceptin are heart problems, infections, lung and blood problems, and reactions related to the way Herceptin is given. In the study comparing Herceptin given under the skin and by infusion into a vein, some side effects have been reported more frequently with Herceptin given under the skin: infections with or without neutropenia (low levels of neutrophils, a type of white blood cells), heart problems, reactions related to the way Herceptin is given and high blood pressure. For the full list of all side effects reported with Herceptin, see the package leaflet.

Herceptin must not be used in people who are hypersensitive (allergic) to trastuzumab, mouse proteins or to any of the other ingredients. It must not be used in patients who have serious breathing problems when they are at rest because of advanced cancer, or who need oxygen therapy.

Herceptin can cause cardiotoxicity (harm to the heart), including heart failure (when the heart does not work as well as it should). Care should be taken if it is given to patients who already have heart problems or high blood pressure, and all patients need to be monitored during and after treatment to check their heart.

Why has Herceptin been approved?

The CHMP decided that Herceptin's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Herceptin:

The European Commission granted a marketing authorisation valid throughout the European Union for Herceptin on 28 August 2000.

The full EPAR for Herceptin can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Herceptin, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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