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Tyverb (*lapatinib*)

An overview of Tyverb and why it is authorised in the EU

What is Tyverb and what is it used for?

Tyverb is a cancer medicine used to treat patients with breast cancer that has been shown to be 'expressing' large amounts of HER2. This means that the cancer produces a specific protein called HER2 (also known as ErbB2) in large quantities on the surface of the cancer cells. Tyverb is used in the following ways:

- in combination with capecitabine (another cancer medicine) when the cancer is advanced or metastatic and got worse following previous treatment including an anthracycline and a taxane (other types of cancer medicine), and following treatment of the patient's metastatic disease with trastuzumab (another cancer medicine). 'Advanced' means that the cancer has started to spread and 'metastatic' means that the cancer has already spread to other parts of the body;
- in combination with trastuzumab for metastatic cancer that does not respond to hormones (hormone receptor-negative disease), and which got worse when previously treated with a combination of trastuzumab and other cancer medicines (chemotherapy);
- in combination with an aromatase inhibitor (another type of cancer medicine) in women who have been through the menopause, when the cancer is metastatic and responds to hormones. This combination is used in women who do not currently need to receive standard chemotherapy to treat their cancer.

Tyverb contains the active substance lapatinib.

How is Tyverb used?

Tyverb can only be obtained with a prescription and should only be started by a doctor who has experience in giving cancer medicines.

Tyverb is available as tablets (250 mg) and the recommended dose is 4 tablets a day when used with trastuzumab, 5 tablets a day when it is used with capecitabine, and 6 tablets a day when taken with an aromatase inhibitor. All of the tablets must be taken together at the same time every day, at least 1 hour before or 1 hour after food.

The doctor may decide to interrupt or stop treatment in patients experiencing certain side effects, especially those affecting the heart, lungs or liver. If patients start to take Tyverb again, they may

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need to use a lower dose. Patients who stop taking Tyverb after developing severe liver problems should not start to take the medicine again.

For more information about using Tyverb, see the package leaflet or contact your doctor or pharmacist.

How does Tyverb work?

The active substance in Tyverb, lapatinib, belongs to a group of medicines called protein kinase inhibitors. These medicines work by blocking enzymes known as protein kinases, which can be found in some receptors (targets) on the surface of cancer cells including HER2. HER2 is a receptor for a substance called epidermal growth factor which stimulates the cancer cells to grow uncontrollably. By blocking HER2 receptors, Tyverb helps to control growth of the cancer. About a quarter of breast cancers produce HER2.

What benefits of Tyverb have been shown in studies?

Tyverb in combination with another cancer medicine was shown to be more effective than the comparator treatment in three main studies involving women with breast cancer. In all the studies, the main measure of effectiveness was how long the patients lived without their disease getting worse, which was assessed in scans. The studies also looked at how long the patients survived.

The first study compared Tyverb in combination with capecitabine, with capecitabine taken alone. It involved 408 women with advanced or metastatic disease that was producing large quantities of HER2 who had already been treated with anthracyclines, taxanes and trastuzumab but whose disease had got worse or come back. The women taking Tyverb in combination with capecitabine lived for an average of 23.9 weeks without their disease getting worse, as assessed by their doctors, compared with 18.3 weeks in the women taking capecitabine alone. Women taking Tyverb with capecitabine survived for an average of 75 weeks, and those taking capecitabine alone survived for an average of 64.7 weeks.

The second study compared Tyverb alone with a combination of Tyverb plus trastuzumab. It involved 296 women with metastatic disease that was producing large quantities of HER2 and got worse despite treatment with trastuzumab and other cancer medicines (including anthracyclines and taxanes). Women taking Tyverb with trastuzumab lived without their disease getting worse for 12.0 weeks on average, compared with 8.1 weeks in those taking Tyverb alone. In addition, women taking the combination survived for 14.0 months on average, compared with 9.5 months in those taking Tyverb alone.

The third study compared Tyverb with placebo (a dummy treatment), both of which were taken together with letrozole (an aromatase inhibitor). It involved 1,286 women who had been through the menopause with metastatic breast cancer that was sensitive to hormones. 219 of the women had cancer that was producing large quantities of HER2. The women had not received trastuzumab or an aromatase inhibitor before entering this study. The women whose cancer was producing large quantities of HER2 taking Tyverb in combination with letrozole survived for an average of 35.4 weeks without their disease getting worse. This compared with 13.0 weeks in those taking placebo in combination with letrozole.

What are the risks associated with Tyverb?

The most common side effects with Tyverb (which may affect more than 1 in 4 patients) are rash and side effects affecting the stomach and gut (such as diarrhoea, nausea (feeling sick) and vomiting).

Palmar-plantar erythrodysaesthesia (rash and numbness on the palms and soles) is also very common when Tyverb is taken with capecitabine. For the full list of side effects and restrictions with Tyverb, see the package leaflet.

Why is Tyverb authorised in the EU?

The European Medicines Agency decided that Tyverb's benefits are greater than its risks and it can be authorised for use in the EU. Tyverb in combination with other cancer medicines has been shown to improve survival of patients with breast cancer that produces large quantities of HER2, and its side effects are considered acceptable.

Tyverb was originally given 'conditional approval'. This means that there was more evidence to come about the effectiveness of the medicine. As the company has supplied the additional information necessary, the authorisation has been switched from conditional to full approval.

What measures are being taken to ensure the safe and effective use of Tyverb?

The company that markets Tyverb will evaluate ways to predict resistance (the medicine becoming less effective) in breast cancer patients taking Tyverb with other cancer medicines.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Tyverb have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Tyverb are continuously monitored. Side effects reported with Tyverb are carefully evaluated and any necessary action taken to protect patients.

Other information about Tyverb

Tyverb received a conditional marketing authorisation valid throughout the EU on 10 June 2008. This was switched to a full marketing authorisation on 17 February 2015.

Further information on Tyverb can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

This overview was last updated in 07-2018.