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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Tyverb (lapatinib)

On 15 February 2012, Glaxo Group Ltd. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a change to the marketing authorisation for Tyverb, to add the use in combination with paclitaxel for the treatment of metastatic breast cancer.

What is Tyverb?

Tyverb is a medicine that contains the active substance lapatinib. It is available as tablets.

Tyverb is used in combination with capecitabine or with an aromatase inhibitor (other anticancer medicines) 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 tumour cells. Tyverb is used when the cancer is advanced or metastatic. 'Advanced' means that the cancer has started to spread and 'metastatic' means that the cancer has already spread to other parts of the body.

Tyverb has been authorised in the EU since June 2008. It has been granted 'conditional' marketing authorisation because there is more evidence to come about the medicine. Tyverb is available in all EU Member States.

What was Tyverb expected to be used for?

Tyverb was also expected to be used in combination with paclitaxel (another anticancer medicine) for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2.

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How is Tyverb expected to work?

Tyverb in combination with paclitaxel is expected to work in the same way as it does in its existing indication. The active substance in Tyverb, lapatinib, belongs to a group of medicines called protein kinase inhibitors. These compounds work by blocking enzymes known as protein kinases, which can be found in some receptors on the surface of cancer cells including HER2. HER2 is a receptor for epidermal growth factor and is involved in stimulating the cells to divide uncontrollably. By blocking these receptors, Tyverb helps to control cell division. About a quarter of breast cancers express HER2.

What did the company present to support its application?

The company presented data from one main study involving a total of 444 patients with metastatic breast cancer that was expressing large quantities of HER2. The study compared Tyverb with placebo (a dummy treatment), both of which were taken together with paclitaxel. The main measure of effectiveness was overall survival (the length of time the patients lived).

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

The application was withdrawn after 'day 90'. This means that the CHMP had evaluated the documentation provided by the company and formulated lists of questions. The CHMP was assessing the company's responses to the questions at the time of the withdrawal. After the CHMP had assessed the company's responses to the 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 response to the CHMP lists of questions, at the time of the withdrawal, the CHMP had concerns and was of the provisional opinion that Tyverb could not have been approved for use in combination with paclitaxel in the treatment of metastatic breast cancer.

The CHMP was concerned that the main study, which compared Tyverb with placebo, did not allow the Committee to conclude on how Tyverb compares with other authorised treatments. In particular, the Committee could not exclude the possibility that Tyverb in combination with paclitaxel is inferior to the standard treatment, trastuzumab plus paclitaxel. A comparative study would have addressed this issue.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the company had not addressed its concerns and that the benefit-risk balance of Tyverb in combination with paclitaxel for the treatment of metastatic breast cancer could not be properly assessed.

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

In its letter notifying the Agency of the withdrawal of application, the company stated that its decision to withdraw the application was based on the CHMP's assessment that the lack of a study comparing Tyverb with another treatment hampered the proper assessment of the benefit-risk balance in European patients in the applied indication.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials using Tyverb at this time.

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 with Tyverb used in combination with capecitabine or with an aromatase inhibitor?

There are no consequences on the use of Tyverb in its authorised indications.

The full European Public Assessment Report for Tyverb can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.