EMA/671281/2015
EMEA/H/C/000316

EPAR summary for the public

Xeloda

capecitabine

This is a summary of the European public assessment report (EPAR) for Xeloda. 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 Xeloda.

What is Xeloda?

Xeloda is a cancer medicine that contains the active substance capecitabine. It is available as tablets (150 and 500 mg).

What is Xeloda used for?

Xeloda is used to treat:

- colon (large bowel) cancer. Xeloda is used with or without other cancer medicines in patients who have had surgery for 'stage III' or 'Dukes' stage C' colon cancer;
- metastatic colorectal cancer (cancer of the large bowel that has spread to other parts of the body). Xeloda is used with or without other cancer medicines;
- advanced gastric (stomach) cancer. Xeloda is used with other cancer medicines, including a platinum-containing cancer medicine such as cisplatin;
- locally advanced or metastatic breast cancer (breast cancer that has begun to spread to other parts of the body). Xeloda is used with docetaxel (another cancer medicine) after treatment with anthracyclines (another type of cancer medicine) has failed. It can also be used on its own when treatment with both anthracyclines and taxanes (another type of cancer medicine) has failed or when repeat treatment with anthracyclines is not suitable for the patient.

The medicine can only be obtained with a prescription.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

How is Xeloda used?

Xeloda should only be prescribed by a doctor who is qualified in the use of cancer medicines.

Xeloda is taken twice a day at doses between 625 and 1,250 mg per square metre body surface area (calculated using the patient's height and weight). The dose depends on the type of cancer being treated. The doctor will calculate the number of 150- and 500 mg tablets the patient needs to take. Xeloda tablets should be swallowed with water within the 30 minutes after a meal.

Treatment is continued for six months after colon surgery. For other types of cancer, treatment is stopped if the disease gets worse or the patient cannot tolerate the treatment. Doses need to be adjusted for patients with liver or kidney disease and for patients who develop certain side effects.

Full details are available in the summary of product characteristics (also part of the EPAR).

How does Xeloda work?

The active substance in Xeloda, capecitabine, is a cytotoxic medicine (a medicine that kills cells that are dividing, such as cancer cells) that belongs to the group 'anti metabolites'. Capecitabine is a 'prodrug' that is converted to 5-fluorouracil (5-FU) in the body, but more is converted in tumour cells than in normal tissues. It is taken as tablets, while 5-FU normally needs to be injected.

5-FU is an analogue of pyrimidine. Pyrimidine is part of the genetic material of cells (DNA and RNA). In the body, 5-FU takes the place of pyrimidine and interferes with the enzymes involved in making new DNA. As a result, it inhibits the growth of tumour cells and eventually kills them.

How has Xeloda been studied?

In colon cancer, Xeloda on its own has been compared with the combination of 5-FU and folinic acid (a medicine that enhances the effects of 5-FU) in 1,987 patients who had previously had surgery for their cancer.

In metastatic colorectal cancer, Xeloda taken on its own has been compared with the combination of 5-FU and folinic acid in two studies involving 1,207 patients. Xeloda has also been compared with the combination of 5-FU and folinic acid, both in combination with oxaliplatin (another cancer medicine), in two studies: the first involved 2,035 patients who had not been treated before, and the second involved 627 patients who had failed previous treatment with irinotecan and a fluoropyrimidine (a group of cancer medicines that includes 5-FU).

In advanced gastric cancer, Xeloda with cisplatin has been compared with a combination of 5-FU and cisplatin in one study involving 316 patients. The company also presented the results of a published study involving 1,002 patients, which compared the effects of Xeloda and 5-FU, taken in combination with platinum-containing medicines and epirubicin (another cancer medicine).

In locally advanced or metastatic breast cancer, Xeloda with docetaxel has been compared with docetaxel on its own in 511 women. Two smaller studies (238 patients) have also looked at the effectiveness of Xeloda after failure of treatment with taxanes and anthracyclines.

The main measures of effectiveness were the number of patients whose cancer responded to treatment, how long it took for the disease to progress, how long the patients remained disease-free or how long they survived.

What benefit has Xeloda shown during the studies?

In colon cancer, Xeloda was also as effective as 5-FU and folinic acid, with about two-thirds of the patients remaining disease-free throughout the 3.8 years of the study.

In metastatic colorectal cancer, Xeloda was as effective as the combination of 5-FU and folinic acid. When taken alone, between 19 and 25% of patients responded to Xeloda, and 12 to 15% responded to the comparator combination. When either Xeloda or 5-FU and folinic acid were taken with oxaliplatin, it took an average of eight months for the disease to get worse in patients who had not been treated before, and five months in patients whose previous treatment had failed.

In advanced gastric cancer, Xeloda with cisplatin was as effective as 5-FU and cisplatin. It took 5.6 months for the disease to get worse in patients taking Xeloda and cisplatin, and 5.0 months in patients receiving 5-FU and cisplatin. The published study showed that patients taking combinations of medicines that included Xeloda survived for a similar length of time as those taking combinations including 5-FU.

In locally advanced or metastatic breast cancer, Xeloda combined with docetaxel was more effective that docetaxel on its own in increasing how long it took for the disease to get worse (186 days compared with 128 days).

What is the risk associated with Xeloda?

The most common side effects with Xeloda (seen in more than 1 patient in 10) are anorexia (loss of appetite), diarrhoea, vomiting, nausea (feeling sick), stomatitis (sores in the mouth), abdominal (tummy) pain, palmar-plantar erythrodysaesthesia syndrome ('hand-foot syndrome', a skin reaction with rash and pain on the hands and feet), fatigue (tiredness) and asthenia (weakness).

For the full list of all side effects reported with Xeloda, see the package leaflet.

Xeloda must not be used in people who may be hypersensitive (allergic) to capecitabine, to any of the other ingredients, or to fluorouracil. Xeloda must also not be used in the following groups:

- patients who have had severe and unexpected reactions to fluoropyrimidine therapy (a group of cancer medicines);
- patients with complete absence of activity of the dihydropyrimidine dehydrogenase enzyme;
- pregnant or breastfeeding women;
- patients with severe leucopenia, neutropenia, or thrombocytopenia (low levels of white cells or platelets in the blood);
- patients with severe liver or kidney disease;
- patients treated with sorivudine or similar cancer medicines such as brivudine within the last four weeks.

Why has Xeloda been approved?

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

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

A risk management plan has been developed to ensure that Xeloda is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Xeloda, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Xeloda

The European Commission granted a marketing authorisation valid throughout the European Union for Xeloda on 2 February 2001.

The full EPAR for Xeloda 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 Xeloda, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 10-2015.