EMA/373967/2020
EMEA/H/C/000316

Xeloda (*capecitabine*)

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

What is Xeloda and what is it used for?

Xeloda is a cancer medicine that is used to treat:

- colon (large bowel) cancer. Xeloda is used on its own or with 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 on its own or with 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 further treatment with anthracyclines is not suitable for the patient.

Xeloda contains the active substance capecitabine.

How is Xeloda used?

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

Before starting treatment, it is recommended that patients are tested to check that they have a working dihydropyrimidine dehydrogenase (DPD) enzyme.

Xeloda is available as tablets (150 and 500 mg). The dose depends on the patient's height and weight and the type of cancer being treated. Xeloda tablets should be taken within 30 minutes after a meal. The tablets are given twice daily for 14 days followed by a 7-day gap before the next course.

Treatment is continued for 6 months after colon surgery. For other types of cancer, treatment is stopped if the disease gets worse or the side effects are unacceptable. Doses need to be adjusted for patients with liver or kidney disease and for patients who develop certain side effects. For patients with partial DPD deficiency, a lower starting dose may be considered.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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

How does Xeloda work?

The active substance in Xeloda, capecitabine, is a cytotoxic medicine (a medicine that kills rapidly dividing cells, such as cancer cells) that belongs to the group 'anti-metabolites'. Capecitabine is converted to the medicine fluorouracil in the body, but more is converted in tumour cells than in normal tissues.

Fluorouracil is very similar to pyrimidine. Pyrimidine is part of the genetic material of cells (DNA and RNA). In the body, fluorouracil takes the place of pyrimidine and interferes with the enzymes involved in making new DNA. As a result, it prevents the growth of tumour cells and eventually kills them.

What benefits of Xeloda have been shown in studies?

Colon cancer

In colon cancer, Xeloda on its own has been shown to be as effective as the combination of fluorouracil and folinic acid (a medicine that enhances the effects of fluorouracil) in a main study involving 1,987 patients who had had surgery for their cancer. About two-thirds of the patients taking Xeloda or the combination remained disease-free throughout the 3.8 years of the study.

Another study involving 1,886 patients who had had surgery showed that Xeloda together with oxaliplatin (another cancer medicine) was more effective than the combination of fluorouracil and folinic acid: patients taking Xeloda and oxaliplatin had 20% lower risk of getting cancer again or death compared with patients taking fluorouracil and folinic acid.

Colorectal cancer

In metastatic colorectal cancer, Xeloda taken on its own was as effective as the combination of fluorouracil and folinic acid in 2 studies involving 1,207 patients. The disease responded in 19 to 25% of patients treated with Xeloda, compared with 12 to 15% with the comparator combination.

Xeloda has also been compared with the combination of fluorouracil and folinic acid, both used in combination with oxaliplatin, in 2 studies: the first involved 2,035 patients who had not been treated before, and the second involved 627 patients in whom previous treatment with irinotecan and a fluoropyrimidine (a group of cancer medicines that includes fluorouracil) had not worked. Results showed that when either Xeloda or fluorouracil and folinic acid were used with oxaliplatin, it took an average of 8 months for the disease to get worse in patients who had not been treated before, and 5 months in patients whose previous treatment had not worked.

Gastric cancer

In advanced gastric cancer, Xeloda with cisplatin was as effective as a combination of fluorouracil and cisplatin in slowing down the disease in a study involving 316 patients. It took 5.6 months for the disease to get worse in patients taking Xeloda and cisplatin, and 5.0 months in patients receiving fluorouracil and cisplatin. In addition, the results of a study involving 1,002 patients showed that patients taking combinations of medicines that included Xeloda survived for a similar period to those taking combinations that included fluorouracil.

Breast cancer

In locally advanced or metastatic breast cancer, Xeloda with docetaxel was more effective than docetaxel on its own in a study involving 511 women. Patients taking Xeloda with docetaxel had a longer time before the disease got worse compared with patients taking docetaxel on its own (186 days compared with 128 days). Two smaller studies (238 patients) showed that Xeloda was effective after treatment with taxanes and anthracyclines did not work.

What are the risks associated with Xeloda?

The most common side effects with Xeloda are diarrhoea, nausea (feeling sick), vomiting, abdominal (belly) pain, stomatitis (sores in the mouth), palmar-plantar erythrodysaesthesia (hand-foot syndrome, a skin reaction with rash and pain on the hands and feet), tiredness, weakness, loss of appetite, problems due to formation of blood clots in the blood vessels, heart problems and kidney problems in patients who already have reduced kidney function. For the full list of 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;
- patients known to have no DPD enzyme activity;
- 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 taking brivudine (an antiviral medicine for treating shingles or chickenpox) or who have taken it in the last 4 weeks.

Why is Xeloda authorised in the EU?

Xeloda has been shown to be effective in treating colon, colorectal, gastric and breast cancer. The safety profile of the medicine is considered acceptable. The European Medicines Agency therefore decided that Xeloda's benefits are greater than its risks and it can be authorised for use in the EU.

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

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

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

Other information about Xeloda

Xeloda received a marketing authorisation valid throughout the EU on 2 February 2001.

Further information on Xeloda can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/Xeloda.

This overview was last updated in 06-2020.