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Cyramza (*ramucirumab*)

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

What is Cyramza and what is it used for?

Cyramza is a cancer medicine used to treat adult patients with:

- gastric cancer (cancer of the stomach) or cancer of the area where the gullet (oesophagus) enters the stomach (known as gastro-oesophageal junction adenocarcinoma);
- metastatic colorectal cancer (cancer of the large bowel that has spread to other parts of the body);
- non-small cell lung cancer that has spread to other parts of the body or in patients whose cancer involves mutations (changes) in proteins called endothelial growth factor receptors (EGFRs);
- hepatocellular carcinoma (a type of liver cancer) in patients with a high blood level of a protein called alpha fetoprotein (AFP).

Cyramza is for use in cancers that are usually advanced or have spread despite other treatment. For most cancers it is used in combination with other medicines.

For detailed information on the use of Cyramza in all conditions, see the package leaflet or contact your doctor or pharmacist.

Cyramza contains the active substance ramucirumab.

How is Cyramza used?

Cyramza is given by infusion (drip) into a vein. It can only be obtained with a prescription and treatment should be started and supervised by a specialist who has experience in the treatment of cancer.

The dose of Cyramza and how often it is given depends on the patient's weight and the condition being treated.

Treatment should continue for as long as the disease remains under control and the patient does not have unacceptable side effects. For more information about using Cyramza, see the package leaflet or contact your doctor or pharmacist.

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How does Cyramza work?

The active substance in Cyramza, ramucirumab, is a monoclonal antibody (a type of protein) designed to attach to vascular endothelial growth factor receptor (VEGFR), a protein present at high levels in tumours. VEGFR helps the development of new blood vessels that supply the tumour. By attaching to VEGFR, ramucirumab blocks this action, reducing the blood supply to the tumour and so slowing the growth of the cancer.

What benefits of Cyramza have been shown in studies?

Cyramza was found effective in patients with advanced gastric or gastro-oesophageal junction cancer, metastatic colorectal cancer, advanced or metastatic non-small cell lung cancer and hepatocellular carcinoma in 6 main studies.

Gastric cancer

In one main study involving 665 patients with advanced gastric or gastro-oesophageal junction cancer which worsened despite treatment with medicines containing platinum and a fluoropyrimidine, those treated with Cyramza and paclitaxel lived longer than patients receiving paclitaxel and placebo (a dummy treatment): on average 9.6 months versus 7.4 months respectively. Similarly, in another study in 355 patients, those treated with Cyramza plus best supportive care lived longer than patients receiving placebo plus best supportive care (an average of 5.2 months versus 3.8 months, respectively).

Colorectal cancer

In a main study involving 1,072 patients with metastatic colorectal cancer which worsened despite treatment with bevacizumab, oxaliplatin and a fluoropyrimidine, those treated with Cyramza and FOLFIRI lived longer than patients receiving FOLFIRI (a combination of fluorouracil, folinic acid and irinotecan) and placebo: on average 13.3 months versus 11.7 months respectively.

Non-small cell lung cancer

In a main study involving 449 patients with metastatic non-small cell lung cancer and EGFR mutation, patients receiving Cyramza with erlotinib lived on average for 19 months without their cancer getting worse, compared with 12 months in patients who received placebo with erlotinib.

In another main study involving 1,253 patients with advanced or metastatic non-small cell lung cancer which worsened despite treatment with medicines containing platinum, those treated with Cyramza and docetaxel lived longer than patients receiving docetaxel and placebo: on average 10.5 months versus 9.1 months respectively.

Hepatocellular carcinoma

In a study involving 292 patients with hepatocellular carcinoma that is advanced or cannot be removed with surgery and who have high AFP blood level and have been previously treated with sorafenib, patients receiving Cyramza lived longer than those receiving placebo: 8.5 versus 7.3 months, respectively.

What are the risks associated with Cyramza?

The most common side effects with Cyramza when used on its own (which may affect more than 1 in 10 people) include peripheral oedema (swelling of the ankles and feet due to fluid retention), high

blood pressure, diarrhoea, abdominal pain, headache, proteinuria (excess protein in the urine) and thrombocytopenia (low blood platelet counts which can lead to bleeding and bruising). The most common side effects when Cyramza is used with chemotherapy are tiredness or weakness, neutropenia (low counts of a particular type of white blood cell), diarrhoea, nosebleeds and stomatitis (inflammation of the lining of the mouth). The most common side effects when Cyramza is used with erlotinib are infections, diarrhoea, high blood pressure, stomatitis, proteinuria, hair loss and nosebleeds.

The most serious adverse effects reported (either of Cyramza alone or in combination with other cancer medicines) include gastrointestinal perforation (a hole that develops in the wall of the gut), severe gastrointestinal haemorrhage (bleeding from the gut) and arterial thromboembolic events (problems caused by blood clots and blockage of the arteries).

For the full list of side effects of Cyramza, see the package leaflet.

When used for lung cancer, Cyramza must not be used when there is a cavity in the cancer or if the cancer is close to a major blood vessel. For the full list of restrictions, see the package leaflet.

Why is Cyramza authorised in the EU?

The European Medicines Agency decided that Cyramza's benefits are greater than its risks and it can be authorised for use in the EU. The Agency noted that Cyramza prolonged the lives of patients with gastric and gastro-oesophageal junction cancer when it was given with paclitaxel. The benefit was smaller when Cyramza was given on its own, but this could still be an option when treatment with paclitaxel is not considered appropriate. Cyramza also prolonged life expectancy or increased the time before the disease worsened in patients with colorectal cancer, non-small cell lung cancer and hepatocellular carcinoma. Although the effects were modest, the size of the benefit was considered clinically relevant given the normally poor prognosis in these patients.

The safety profile of Cyramza is in line with that expected for other medicines blocking VEGFR activity and is considered manageable.

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

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

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

Other information about Cyramza

Cyramza received a marketing authorisation valid throughout the EU on 19 December 2014.

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

This overview was last updated in 01-2020.