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EPAR summary for the public

Cometriq

cabozantinib

This is a summary of the European public assessment report (EPAR) for Cometriq. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Cometriq.

For practical information about using Cometriq, patients should read the package leaflet or contact their doctor or pharmacist.

What is Cometriq and what is it used for?

Cometriq is a cancer medicine that contains the active substance cabozantinib. It is used to treat adults with medullary thyroid cancer, a type of cancer originating in the cells in the thyroid gland that produce the hormone calcitonin. Cometriq is used when the cancer cannot be removed by surgery and has progressed or spread to other parts of the body.

The benefits of Cometriq may be smaller for patients whose cancer does not have a mutation in a gene called the 're-arranged during transfection' (RET) gene, and this should be taken into account when deciding whether to start treatment.

Because the number of patients with medullary thyroid cancer is low, the disease is considered 'rare', and Cometriq was designated an 'orphan medicine' (a medicine used in rare diseases) on 6 February 2009.

How is Cometriq used?

Cometriq can only be obtained with a prescription and treatment should only be started by a doctor who has experience in using cancer medicines.

Cometriq is available as capsules (20 and 80 mg). The recommended dose is 140 mg once a day, taken as one 80-mg and three 20-mg capsules. Patients should not eat for at least two hours before and one hour after their dose of Cometriq. The dose may need to be reduced or stopped temporarily

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due to side effects, especially during the first eight weeks of therapy. Treatment is continued until the patient no longer benefits from it or side effects become unacceptable.

Cometriq should be used with care in patients taking certain other medicines that affect the way it is broken down in the body. For further information, see the package leaflet.

How does Cometriq work?

The active substance in Cometriq, cabozantinib, is a tyrosine kinase inhibitor. This means that it blocks the activity of enzymes known as tyrosine kinases. These enzymes can be found in certain receptors (such as VEGF, MET and RET receptors) in cancer cells, where they activate several processes including cell division and the growth of new blood vessels to supply the cancer. By blocking the activity of these receptors in cancer cells, the medicine reduces the growth and spread of the cancer.

What benefits of Cometriq have been shown in studies?

Cometriq has been shown to be effective in one main study involving 330 adults with medullary thyroid cancer that could not be treated with surgery and was extensive or had spread to other parts of the body. Cometriq was given once a day in an initial dose of 140 mg (reduced if necessary due to side effects) and compared with placebo (a dummy treatment). The main measure of effectiveness was progression-free survival (how long the patients lived before their disease got worse): in patients given Cometriq this was 11.2 months, compared with 4.0 months in those given placebo.

What are the risks associated with Cometriq?

The most common side effects with Cometriq (which may affect more than 2 in 10 people) are diarrhoea, palmar-plantar erythrodysaesthesia syndrome (hand-foot syndrome, which involves rash and numbness on the palms and soles), loss of weight, loss of appetite, nausea (feeling sick), tiredness, taste disturbances, changes in hair colour, hypertension (high blood pressure), inflammation of the mucosa (moist tissue that lines certain body cavities) including stomatitis (inflammation of the lining of the mouth), constipation, vomiting, weakness, and changes in the sound of the voice. The most common abnormal results in laboratory blood tests were increased liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP), low white cell counts (lymphopenia or neutropenia), thrombocytopenia (low blood-platelet counts), hypocalcaemia (low blood calcium levels), hypophosphataemia (low blood levels of phosphates), hypomagnesaemia (low blood magnesium levels), hypokalaemia (low blood potassium levels) and hyperbilirubinaemia (increased amounts of bilirubin, a breakdown product of red blood cells).

The most common serious side effects are pneumonia, inflammation of the mucosa, hypocalcaemia (low calcium levels in the blood), dysphagia (difficulty swallowing), dehydration, pulmonary embolism (blood clots in the vessels supplying the lungs), and hypertension. For the full list of all side effects and restrictions with Cometriq, see the package leaflet.

Why is Cometriq approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Cometriq's benefits are greater than its risks and recommended that it be approved for use in the EU. Cometriq had shown a benefit in patients with advanced medullary thyroid cancer unsuitable for surgery, who have few other treatment options. The side effects were considered manageable and were acceptable, compared with the limited other treatment options available. However, the Committee noted that

many patients required reductions in their dose and recommended that the company should study whether starting at lower doses would still be effective but would have fewer side effects.

Cometriq has been given 'conditional approval'. This means that there is more evidence to come about the medicine, which the company is required to provide. Every year, the European Medicines Agency will review any new information that becomes available and this summary will be updated as necessary.

What information is still awaited for Cometriq?

Since Cometriq has been granted a conditional approval, the company that markets Cometriq will provide information from a study comparing the safety and effectiveness of different doses of Cometriq, and its benefit in patients lacking the RET gene mutation or whose cancer has changes in another family of genes called RAS.

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

A risk management plan has been developed to ensure that Cometriq 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 Cometriq, including the appropriate precautions to be followed by healthcare professionals and patients.

Further information can be found in the summary of the risk management plan.

Other information about Cometriq

The European Commission granted a marketing authorisation valid throughout the European Union for Cometriq on 21 March 2014.

The full EPAR and risk management plan summary for Cometriq 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 Cometriq, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Cometriq can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 07-2015.