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EPAR summary for the public

Stivarga

regorafenib

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

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

What is Stivarga and what is it used for?

Stivarga is a cancer medicine that contains the active substance regorafenib. It is used on its own to treat the following cancers:

- colorectal cancer (cancer of the bowel and rectum) that has spread to other parts of the body;
- gastrointestinal stromal tumour (GIST, a cancer of the stomach and bowel) that has spread or cannot be surgically removed;
- hepatocellular carcinoma (HCC, a cancer of the liver).

Stivarga is used in patients who have already been treated with, or who cannot be given, other available treatments. For colorectal cancer, these include chemotherapy based on medicines called fluoropyrimidines and treatment with other cancer medicines known as anti-VEGF and anti-EGFR therapies. Patients with GIST should have tried treatment with imatinib and sunitinib and patients with HCC should have tried sorafenib before starting treatment with Stivarga.

How is Stivarga used?

Treatment with Stivarga must be prescribed by a doctor who is experienced in treating cancer. The medicine can only be obtained with a prescription.

Stivarga is available as tablets (40 mg). It is taken in 4-week treatment cycles at a recommended starting dose of 160 mg (4 tablets) once every day for three weeks, followed by a week without taking the medicine. Doses should be taken at the same time each day with a light meal. Treatment should

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continue for as long as the patient benefits from treatment or until the side effects become too severe. Treatment may need to be interrupted or stopped, or the dose reduced, if the patient experiences certain side effects. For further information, see the package leaflet.

How does Stivarga work?

The active substance in Stivarga, regorafenib, is a 'protein kinase inhibitor'. This means that it blocks several enzymes that are important for the development of a blood supply to tumours and the growth and development of cancer cells. By blocking the action of these enzymes, Stivarga helps to stop the growth and spread of the cancer.

What benefits of Stivarga have been shown in studies?

Colorectal cancer

In a main study involving 760 patients with metastatic colorectal cancer which had progressed after standard therapy, Stivarga was compared with placebo (a dummy treatment) and the main measure of effectiveness was overall survival (the length of time that patients lived). All patients also received supportive care, including pain medicines and treatment for infections. The study showed that Stivarga improved survival, with treated patients living for 6.4 months on average, compared with 5 months for those given placebo.

GIST

In another main study, Stivarga was compared with placebo in 199 patients with GIST that had spread or was inoperable and who were also given best supportive care. Supportive care included treatments like pain relief, antibiotics, and blood transfusions that help the patient but without treating the cancer. The study showed that Stivarga with supportive care was effective at prolonging the length of time patients lived without their disease getting worse. Patients treated with Stivarga lived on average for 4.8 months without their disease getting worse compared with 0.9 months for patients taking placebo and supportive care.

HCC

In a main study involving 573 patients with HCC that had worsened after treatment with sorafenib, Stivarga was compared with placebo and the main measure of effectiveness was overall survival. All patients also received supportive care. The study showed that Stivarga increased the length of time that patients lived overall, with patients treated with Stivarga living for 10.6 months on average, compared with 7.8 months for those given placebo.

What are the risks associated with Stivarga?

The most common side effects with Stivarga (which may affect more than 3 in 10 people) are pain, weakness, tiredness, loss of appetite and eating less, hand-foot syndrome (rash and numbness affecting the palms and soles), diarrhoea, infection and hypertension (high blood pressure). The most serious side effects are severe liver injury, bleeding, gastrointestinal perforation (development of a hole in the wall of the gut) and infection.

For the full list of all restrictions and side effects with Stivarga, see the package leaflet.

Why is Stivarga approved?

The European Medicines Agency decided that Stivarga's benefits are greater than its risks and recommended that it be approved for use in the EU. The Committee noted that in colorectal cancer the benefits in terms of extending patient survival were modest, but considered that they outweighed the risks in patients for whom there are no other remaining treatment options. However, given the side effects, the CHMP considered it important to find ways to identify any subgroups of patients who are more likely to respond to Stivarga.

With regard to GIST and HCC, the Committee noted that the outlook is poor for patients whose disease gets worse despite previous treatment. Stivarga had been shown to delay the worsening of the disease in these patients. For patients with HCC, this led to an improvement in the length of time patients lived. The side effects of Stivarga are manageable.

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

The company that markets Stivarga will carry out studies to look for ways of identifying patients who are more likely to respond to treatment.

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

Other information about Stivarga

The European Commission granted a marketing authorisation valid throughout the European Union for Stivarga on 26 August 2013.

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

This summary was last updated in 07-2017.