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Ayvakyt (*avapritinib*)

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

What is Ayvakyt and what is it used for?

Ayvakyt is a cancer medicine used to treat gastrointestinal stromal tumour (GIST), a cancer of the stomach and bowel, that cannot be removed by surgery and has spread to other parts of the body. Ayvakyt is used when the cancer cells have a D842V mutation, a change in the gene for the platelet-derived growth factor receptor alpha (PDGFRA).

Ayvakyt is also used in adults with advanced systemic mastocytosis, which means any of the following disorders of a type of white blood cell known as mast cells: aggressive systemic mastocytosis, systemic mastocytosis associated with a haematological neoplasm (blood cancer), or mast cell leukaemia. It is used after the patient has received at least one systemic treatment (treatment with medicines affecting the whole body).

These diseases are rare, and Ayvakyt was designated an 'orphan medicine' (a medicine used in rare diseases) on 17 July 2017 (GIST) and on 26 October 2018 (mastocytosis).

Ayvakyt contains the active substance avapritinib.

How is Ayvakyt used?

Ayvakyt is available as tablets to be taken by mouth and can only be obtained with a prescription. Treatment should be started and supervised by a specialist doctor experienced in the use of cancer treatments.

Ayvakyt should be taken on an empty stomach. The recommended dose is 300 mg once a day for GIST and 200 mg once a day for advanced systemic mastocytosis. The dose may need to be reduced if the patient is taking other medicines called 'CYP3A inhibitors' that could interfere with the way Ayvakyt is broken down in the body. Treatment may be paused, stopped or the dose reduced if the patient experiences certain side effects.

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

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How does Ayvakyt work?

Ayvakyt is one of a group of medicines called receptor tyrosine kinase inhibitors. It works by blocking the activity of receptors (targets) called PDGFRA on the surface of GIST or mast cells. These receptors help to control cell growth and can be abnormal (mutated) in GIST and mast cells, causing the cells to multiply uncontrollably. By blocking the action of the abnormal receptor, the medicine is expected to help to slow down the growth of these cells.

What benefits of Ayvakyt have been shown in studies?

GIST

Ayvakyt showed benefit in one main study involving 38 patients with GIST where the cancer cells had the D842V PDGFRA mutation. In the study, in which Ayvakyt was not compared with any other medicine, the disease responded to treatment in 95% of patients (36 out of 38) and it took on average 22 months before the cancer got worse in treated patients.

Advanced systemic mastocytosis

For advanced systemic mastocytosis, Ayvakyt showed benefit in one ongoing main study: out of 47 patients with advanced systemic mastocytosis who received previous systemic therapy, 28 (60%) responded to treatment with Ayvakyt. Although patients have been followed for a limited period it is expected that response will last on average for at least 12 months.

What are the risks associated with Ayvakyt?

In patients with GIST, the most common side effects with Ayvakyt (affecting more than 20 in 100 people) are nausea (feeling sick), tiredness, anaemia (low red blood cell counts), periorbital, face or peripheral oedema (swelling of the eyes, face, ankles or feet), hyperbilirubinaemia (high blood levels of bilirubin indicating liver problems), diarrhoea, vomiting, increased lacrimation (watery eyes), decreased appetite and memory impairment (forgetfulness).

The most common serious side effects with Ayvakyt in patients with GIST (which may affect up to 6 in 100 people) are anaemia and pleural effusion (fluid around the lungs).

In patients with advanced systemic mastocytosis , the most common side effects (affecting more than 20 in 100 people) are periorbital and peripheral oedema, thrombocytopenia (low blood platelet counts) and anaemia.

The most common serious side effects (which may affect up to 2 in 100 people) are subdural haematoma (collection of blood between the skull and surface of the brain), anaemia and bleeding.

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

Why is Ayvakyt authorised in the EU?

The European Medicines Agency decided that Ayvakyt's benefits are greater than its risks and it can be authorised for use in the EU.

Ayvakyt benefited a high proportion of patients with GIST with a D842V PDGFRA mutation for a significant length of time. Similar results have not been seen before and are better than those reported in the literature for other medicines of the same type in this patient population, who do not have a lot of treatment options. Although Ayvakyt also had substantial side effects, these were mostly similar to those of other medicines of the same type and were considered manageable.

For advanced systemic mastocytosis, where treatment options are also limited, the benefits were promising and clinically meaningful while the overall safety profile appears consistent with that seen for GIST.

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

What information is still awaited for Ayvakyt?

Since Ayvakyt has been given conditional authorisation, the company that markets Ayvakyt will provide additional results on the safety and effectiveness of the medicine from 2 ongoing studies in GIST, and will also carry out a study of the medicine as it is used by patients with GIST in the real-life setting.

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

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

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

Other information about Ayvakyt

Ayvakyt received a conditional marketing authorisation valid throughout the EU on 24 September 2020.

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

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