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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 adults with 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 to treat systemic mastocytosis, a blood disorder where the body makes too many abnormal mast cells (a type of white blood cell), which can build up in the skin, bones, joints, lymph nodes, liver, spleen, the stomach and gut.

It is used to treat the following advanced forms of systemic mastocytosis: 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).

Ayvakyt is also used to treat adults with moderate to severe symptoms of indolent systemic mastocytosis (ISM), a slow-growing form of systemic mastocytosis. It is used if the patient has not responded to symptomatic treatment (treatment that eases the symptoms of a disease without addressing its cause).

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 can only be obtained with a prescription and treatment should be started and supervised by a doctor experienced in the diagnosis and treatment of either GIST, advanced systemic mastocytosis or ISM.

Ayvakyt is available as tablets to be taken by mouth on an empty stomach. The recommended dose depends on the disease being treated. For patients who are taking other medicines called 'CYP3A inhibitors', concomitant use may need to be avoided or a lower dose may need to be used as these

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medicines could interfere with the way Ayvakyt is broken down in the body. Treatment with Ayvakyt 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.

How does Ayvakyt work?

Ayvakyt belongs to a group of medicines called receptor tyrosine kinase inhibitors. It works by blocking the activity of receptor tyrosine kinase proteins called PDGFRA and KIT that are found on the surface of GIST or mast cells. These proteins 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 proteins, the medicine is expected to help slow down the growth of the GIST or mast cells.

What benefits of Ayvakyt have been shown in studies?

Gastrointestinal stromal tumour

Ayvakyt showed benefit in one main study involving 38 patients with GIST where the cancer cells had a mutation (change) in the PDGFRA protein called a D842V 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.

Indolent systemic mastocytosis

Ayvakyt was shown to be effective at reducing the severity of ISM symptoms in an ongoing study involving 212 patients with moderate to severe ISM that had not responded to symptomatic treatment. The study compared Ayvakyt with placebo (dummy treatment). All patients also received treatment to manage their disease symptoms, which was determined by their doctor. The severity of ISM symptoms was evaluated using the total symptom score (TSS) from the ISM-Symptom Assessment Form, a scoring system that assesses the severity of 11 ISM symptoms. After 24 weeks of treatment, patients treated with Ayvakyt had on average a 16% reduction in their TSS score compared with 9% for those who received placebo. After 24 weeks of treatment, around 53% of patient treated with Ayvakyt achieved the target of at least a 50% reduction in the levels of mast cells or aggregates (build-up) of mast cells in the bone marrow.

What are the risks associated with Ayvakyt?

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

In patients with GIST, the most common side effects with Ayvakyt (affecting more than 20 in 100 people) include 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) include 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) include 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) include subdural haematoma (collection of blood between the skull and surface of the brain), anaemia and bleeding.

In patients with ISM, the most common side effects (which may affect more than 10 in 100 people) include peripheral oedema.

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.

For ISM, Ayvakyt was shown to decrease both the severity of symptoms and the abnormal level of mast cells in patients. At the time of authorisation, there were no approved treatments that treat the underlying cause or had an impact on the course of ISM. No new safety concerns were identified with Ayvakyt when used in the treatment of ISM. While some uncertainties remain regarding the long-term safety and effectiveness of Ayvakyt in the treatment of ISM these will be addressed by further data in the ongoing study in ISM patients.

Ayvakyt has been given 'conditional authorisation'. This means that that the European Medicines Agency decided that the benefits of Ayvakyt are greater than its risks, but the company will have to provide additional evidence after authorisation.

Conditional authorisation is granted on the basis of less comprehensive data than are normally required. It is granted for medicines that fulfil an unmet medical need to treat serious diseases and when the benefits of having them available earlier outweigh any risks associated with using the medicines while waiting for further evidence. Every year, the Agency will review any new information that becomes available until data become comprehensive and this overview will be updated as necessary.

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 a study of the Ayvakyt 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.

This overview was last updated in 01-2024.