

Package leaflet: Information for the patient

AYVAKYT 200 mg film-coated tablets avapritinib

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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2. What you need to know before you take AYVAKYT
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1. What AYVAKYT is and what it is used for

What AYVAKYT is

AYVAKYT is a medicine containing the active substance avapritinib.

What AYVAKYT is used for

AYVAKYT is used in adults to treat:

- a type of digestive tract cancer called gastrointestinal stromal tumour (GIST), when it cannot be treated with surgery (unresectable) or has spread to other parts of the body (metastatic) and that has a specific mutation (D842V) in the gene for platelet-derived growth factor receptor alpha (PDGFRA) protein kinase.
- aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN), or mast cell leukaemia (MCL). These are disorders in which the body produces too many mast cells, a type of white blood cell. Symptoms are caused when too many mast cells enter various organs of your body, such as the liver, bone marrow or spleen. These mast cells also release substances such as histamine which cause various general symptoms that you may be experiencing as well as damage to involved organs. ASM, SM-AHN and MCL are collectively referred to as advanced systemic mastocytosis (AdvSM).

How AYVAKYT works

AYVAKYT stops the activity of a group of proteins in the body called kinases. Mast cells in patients with AdvSM or cells that make up the cancer usually have changes (mutations) in the genes involved in making specific kinases associated with the growth and spread of these cells.

If you have any questions about how AYVAKYT works or why this medicine has been prescribed for you, please ask your doctor.

2. What you need to know before you take AYVAKYT

Do not take AYVAKYT:

- if you are allergic to avapritinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking AYVAKYT:

- **if you have suffered a vascular aneurysm** (bulging and weakening of a blood vessel wall) or **bleeding in your brain** in the last year.
- **if you have low platelet counts.**

Take special care with this medicine:

- You may develop symptoms such as **severe headache, vision problems, severe sleepiness, or severe weakness on one side of your body (signs of bleeding in your brain)**. If these occur, contact your doctor immediately and temporarily stop treatment. For patients with AdvSM, your doctor will evaluate your platelet counts before you start treatment and monitor them as needed during your treatment with avapritinib.
- Treatment with this medicine may lead to a **higher risk of bleeding**. Avapritinib can cause bleeding in the digestive system such as stomach, rectum or intestine. In patients with GIST, avapritinib can also cause bleeding in the liver, as well as bleeding of the tumour. Tell your doctor if you had or have any bleeding problems and if you are taking warfarin, phenprocoumon, rivaroxaban, dabigatran, apixaban, edoxaban or another medicine that thins the blood to prevent blood clots. Before you start taking avapritinib your doctor may decide to do blood tests. Get medical help immediately, if you get the following symptoms: passing blood in the stools or passing black stools, stomach pain, coughing/vomiting up blood.
- You may also develop **memory loss, changes in memory, or be confused (signs of a cognitive effect)**. Avapritinib can sometimes change how you think and how you remember information. Contact your doctor in case you experience these symptoms or in case a family member, caregiver or someone who knows you notices that you are getting forgetful or confused.
- During treatment with this medicine, tell your doctor straight away **if you put on weight very quickly, develop swelling of your face or limbs, have difficulty breathing or become short of breath**. This medicine may cause your body to retain water (severe fluid retention).
- Avapritinib may cause **abnormality of your heart rhythm**. Your doctor may conduct tests to evaluate these problems during your treatment with avapritinib. Tell your doctor if you feel dizzy, faint, or have abnormal heartbeats while taking this medicine.
- You may get **severe stomach and bowel problems (diarrhoea, nausea and vomiting)**. Get medical help immediately if you experience these symptoms.
- You may become **more sensitive to the sun** while taking this medicine. It is important to cover sun-exposed areas of skin and use sunscreen with high sun protection factor (SPF).

While you are taking avapritinib, your doctor will ask you to have regular blood tests. You will also be weighed regularly.

For more information see section 4.

Children and adolescents

AYVAKYT has not been studied in children and adolescents under age 18. Do not give this medicine to children or adolescents under the age of 18 years.

Other medicines and AYVAKYT

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. AYVAKYT may affect the way other medicines work, and certain other medicines may affect how this medicine works.

Tell your doctor or pharmacist before taking AYVAKYT if you are taking any of the following medicines:

The following medicines can increase the effects of avapritinib and may increase its side effects:

- Boceprevir – used to treat hepatitis C
- Cobicistat, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir – used to treat HIV infections/AIDS
- Clarithromycin, erythromycin, telithromycin – used to treat bacterial infections
- Itraconazole, ketoconazole, posaconazole, voriconazole – used to treat serious fungal infections
- Conivaptan – used to treat low blood sodium levels (hyponatraemia)

The following medicines can reduce the effects of avapritinib:

- Rifampicin – used to treat tuberculosis (TB) and some other bacterial infections
- Carbamazepine, phenytoin, fosphenytoin, primidone, phenobarbital – used to treat epilepsy
- St. John's wort (*Hypericum perforatum*) – an herbal medicine used for depression
- Bosentan – used to treat high blood pressure
- Efavirenz and etravirine – used to treat HIV infections/AIDS
- Modafinil – used to treat sleep disorders
- Dabrafenib – used to treat certain cancers
- Nafcillin – used to treat certain bacterial infections
- Dexamethasone – used to reduce inflammation

This medicine may affect how well the following medicines work or increase their side effects:

- Alfentanil, fentanyl – used to control pain during operations and medical procedures
- Atazanavir – used to treat HIV infection/AIDS
- Midazolam – used for anaesthesia, sedation or to decrease anxiety
- Simvastatin – used to treat high cholesterol
- Sirolimus, tacrolimus, ciclosporin – used to prevent organ transplant rejection
- Dihydroergotamine, ergotamine – used to treat migraines and cluster headaches
- Pimozide – used to treat psychosis and Tourette disorder
- Amiodarone – used to treat heart rhythm problems
- Citalopram, escitalopram – used to treat depression
- Ondansetron – used to treat nausea or vomiting

Ask your doctor or pharmacist for advice before taking any medicine.

AYVAKYT with food and drink

You should not drink grapefruit juice or eat grapefruit while on treatment with AYVAKYT.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

This medicine is not recommended for use during pregnancy unless clearly necessary. Avoid becoming pregnant while being treated with this medicine as it may harm your unborn baby. Your doctor will discuss with you the potential risks of taking AYVAKYT during pregnancy.

Your doctor may check if you are pregnant before you start treatment with this medicine.

Women who are able to become pregnant should use effective contraception during treatment and for at least 6 weeks after completion of treatment. Males with female partners who are able to get pregnant should use effective contraception during treatment and for at least 2 weeks after completion of treatment. Talk to your doctor about effective contraception methods that may be right for you.

Breast-feeding

Tell your doctor if you are breast-feeding or planning to breast-feed. It is not known if AYVAKYT passes into breast milk. You should not breast-feed during treatment with this medicine and for at least 2 weeks following the last dose. Talk to your doctor about the best way to feed your baby during this time.

Driving and using machines

AYVAKYT may cause symptoms that affect your ability to concentrate and react (see section 4). Therefore, AYVAKYT may influence the ability to drive and use machines. Take special care when driving a car or operating machines if you experience these side effects.

AYVAKYT contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium-free”.

3. How to take AYVAKYT

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Which strength of AYVAKYT to use

The recommended dose of AYVAKYT will depend on your illness – see below.

AYVAKYT is available in different strength tablets. The strengths are 25 mg, 50 mg, 100 mg, 200 mg and 300 mg. Your doctor will advise you about the strength and number of tablets you should take:

Treatment of GIST

The recommended dose is 300 mg by mouth once daily.

Treatment of AdvSM

The recommended dose is 200 mg by mouth once daily.

If you have liver problems, your doctor may start you on a lower dose of AYVAKYT.

If you get side effects, your doctor may change your dose, temporarily stop, or permanently stop treatment. Do not change your dose or stop taking AYVAKYT unless your doctor tells you to.

Swallow the AYVAKYT tablet(s) whole with a glass of water, on an empty stomach. Do not eat for at least 2 hours before and at least 1 hour after taking AYVAKYT.

If you vomit after taking a dose of AYVAKYT, do not take an extra dose. Take your next dose at your scheduled time.

If you take more AYVAKYT than you should

If you have accidentally taken too many tablets, talk to your doctor straight away. You may require medical attention.

If you forget to take AYVAKYT

If you miss a dose of AYVAKYT, take it as soon as you remember unless your next scheduled dose is due within 8 hours. Take the next dose at your regular time.

Do not take two doses within 8 hours to make up for a forgotten dose.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Most serious side effects

Some side effects may be serious. Tell your doctor straight away if you get any of the following (see also section 2.):

- severe headache, vision problems, severe sleepiness, severe weakness on one side of your body (signs of bleeding in your brain)
- memory loss, changes in memory, or confusion (signs of a cognitive effect)

Other side effects in patients with GIST may include

Very common (may affect more than 1 in 10 people):

- decreased appetite
- memory loss, changes in memory, or confusion (cognitive effects)
- dizziness
- altered taste
- increased tear production
- abdominal (belly) pain
- nausea, retching and vomiting
- diarrhoea
- dryness affecting eyes, lips, mouth and skin
- heartburn
- change in hair colour
- rash
- swelling (e.g. feet, ankle, face, eye, joint)
- tiredness
- blood tests showing decrease in red blood cells (anaemia) and white blood cells
- blood tests showing increased stress on the liver and high levels of bilirubin, a substance produced by the liver

Common (may affect up to 1 in 10 people):

- red, or painful eye, blurry vision
- dehydration
- low albumin in the blood
- depression
- anxiety
- trouble falling asleep (insomnia)
- bleeding in your brain
- decreased sensation, numbness, tingling, or increased sensitivity to pain in arms and legs
- feeling weak or unusually sleepy
- speech disorder or hoarse voice
- movement disorder
- headache
- tremor
- bleeding in the eye
- increased sensitivity to light
- increased blood pressure

- shortness of breath
- stuffy nose
- cough including cough that produces mucus
- gastrointestinal bleed
- increased fluid in the abdomen
- constipation, flatulence (gas)
- difficulty swallowing
- painful mouth, lips or tongue, thrush
- increase in saliva production
- red or itchy skin
- skin discolouration
- hair loss
- pain
- muscle spasms
- blood in urine
- fever or feeling of general discomfort
- changes in the electric activity of the heart
- weight gain or loss
- blood tests showing low blood platelets, often associated with easy bruising or bleeding
- blood tests showing altered amounts of blood minerals
- blood tests showing decreased kidney function
- blood tests showing increased break down of muscle

Uncommon (may affect up to 1 in 100 people):

- bleeding in the tumour
- fluid around the heart
- bleeding in the liver

Other side effects in patients with AdvSM may include

Very common (may affect more than 1 in 10 people):

- altered taste
- memory loss, changes in memory, or confusion (cognitive effects)
- diarrhoea
- nausea and retching
- change in hair colour
- swelling (e.g. feet, ankle, face, eye, joint)
- tiredness
- blood tests showing low blood platelets, often associated with easy bruising or bleeding
- blood tests showing decrease in red blood cells (anaemia) and white blood cells

Common (may affect up to 1 in 10 people):

- headache
- dizziness
- decreased sensation, numbness, tingling, or increased sensitivity to pain in arms and legs
- bleeding in your brain
- increased tear production
- nose bleed
- fluid around your lungs
- vomiting
- heartburn
- increased fluid in the abdomen
- dryness affecting eyes, lips, mouth and skin
- constipation
- abdominal (belly) pain

- gastrointestinal bleed
- rash
- hair loss
- joint pain
- pain
- weight gain
- changes in the electric activity of the heart
- bruising
- blood tests showing increased stress on the liver and high levels of bilirubin, a substance produced by the liver

Uncommon (may affect up to 1 in 100 people):

- fluid around the heart
- red or itchy skin

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at <https://yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store AYVAKYT

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle label and outer carton after "EXP". The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not use this medicine if you notice that the bottle is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What AYVAKYT contains

- The active substance is avapritinib. Each film-coated tablet contains 200 mg avapritinib.
- The other ingredients are:
 - The tablet core contains: microcrystalline cellulose, copovidone, croscarmellose sodium and magnesium stearate (see section 2 "AYVAKYT contains sodium").
 - The tablet coating contains: talc, macrogol 3350, poly(vinyl alcohol), and titanium dioxide (E171).
 - The printing ink contains: Shellac glaze 45% (20% esterified) in ethanol, Brilliant blue FCF (E133), titanium dioxide (E171), black iron oxide (E172) and propylene glycol.

What AYVAKYT looks like and contents of the pack

AYVAKYT 200 mg film-coated tablets are oval, white tablets of 16 mm in length and 8 mm in width, printed with blue ink "BLU" on one side and "200" on the other.

AYVAKYT is supplied in a bottle containing 30 film-coated tablets. Each carton contains one bottle.

Keep the desiccant canister in the bottle.

Marketing Authorisation Holder and Manufacturer

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This medicine has been given ‘conditional approval’.

This means that there is more evidence to come about this medicine.

The Medicines and Healthcare products Regulatory Agency (MHRA) will review new information on this medicine at least every year and this leaflet will be updated as necessary.