

### **Patient leaflet in accordance with the Pharmacists’ Regulations (Preparations) – 1986**

This medicine is dispensed with a doctor’s prescription only

## **AYVAKIT 25 MG TABLETS**

## **AYVAKIT 50 MG TABLETS**

## **AYVAKIT 100 MG TABLETS**

## **AYVAKIT 200 MG TABLETS**

## **AYVAKIT 300 MG TABLETS**

### **Name of active ingredient and quantity in a dosage unit:**

Avapritinib 25 mg

Avapritinib 50 mg

Avapritinib 100 mg

Avapritinib 200 mg

Avapritinib 300 mg

For a list of inactive ingredients and allergens in this medicine: see section 6, “Additional information” in this leaflet.

**Read the entire leaflet carefully before you start using this medicine.** This leaflet contains concise information about this medicine. If you have any further questions, consult the doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

### **1. What is this medicine intended for?**

- **100, 200 and 300 mg:**

For treatment of adults with a certain type of gastrointestinal cancer (in the stomach, bowel or esophagus) called gastrointestinal stromal tumor (GIST) that cannot be removed by surgery or that has spread to other parts of the body (metastatic). The disease is caused by a mutation in the PDGFRA (platelet-derived growth factor receptor alpha) gene.

- **25, 50, 100, and 200 mg:**

For treatment of adults with advanced systemic mastocytosis (AdvSM), including: Aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL).

AYVAKIT is not recommended for the treatment of AdvSM in patients with low platelet counts (less than 50X10<sup>9</sup>/L).

For treatment of GIST your healthcare provider will perform a test to make sure that you have this abnormal PDGFRA gene and that AYVAKIT is right for you.

**Therapeutic group:** AYVAKIT inhibits the activity of a group of proteins in the body called protein kinases. Protein kinases are involved in cell functioning. Overactivity of these protein kinases may lead to certain diseases. AYVAKIT inhibits specific protein kinases.

### **2. Before using this medicine**

#### **Do not use this medicine if:**

You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (see section 6 “Additional information”).
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#### **Before taking AYVAKIT, tell your doctor if:**

- You have low platelet counts
- You suffer from bulging or weakening of a blood vessel wall (aneurysm) or have suffered in the past from bleeding in your brain
- You had a stroke within the last year
- You are pregnant or plan to become pregnant. AYVAKIT can cause harm to your unborn baby. See section “Pregnancy, breastfeeding, and fertility”
- You are breastfeeding or plan to breastfeed. See section “Pregnancy, breastfeeding, and fertility”

#### **Children and adolescents:**

This medicine is not intended for children and adolescents under 18 years old. No information on the product’s efficacy or safety is available in this age group.

#### **Tests and follow-up:**

Your doctor may order a blood count before and during the treatment with AYVAKIT.

#### **Drug interactions:**

**If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.**

AYVAKIT may affect the way other medicines work, and certain other medicines may affect how AYVAKIT works.

There are medicines that can increase the effect of AYVAKIT and may increase its side effects, for example: itraconazole, fluconazole.

There are medicines that can reduce the effect of AYVAKIT, for example: rifampin, efavirenz.

#### **Using this medicine and food:**

Take AYVAKIT on an empty stomach at least one hour before or at least two hours after a meal.

#### **Pregnancy, breastfeeding, and fertility:**

##### Pregnancy

If you are pregnant, think you may be pregnant, or plan to become pregnant, consult your doctor before starting AYVAKIT. AYVAKIT might harm the fetus.

**Women** who are able to become pregnant:

- Your doctor will refer you for a pregnancy test before you start treatment with AYVAKIT.
- You should use effective birth control (contraception) during treatment with AYVAKIT and for 6 weeks after the final dose of AYVAKIT. Consult your doctor about effective birth control methods that may be right for you.
- Tell your doctor right away if you become pregnant or think you may be pregnant during treatment with AYVAKIT.

**Men** with female partners who are able to become pregnant should use effective birth control (contraception) during treatment with AYVAKIT and for 6 weeks after the final dose of AYVAKIT.

##### Breastfeeding

If you are breastfeeding or plan to breastfeed, consult your doctor before starting AYVAKIT.

It is not known if AYVAKIT passes into breast milk.

Do not breastfeed during treatment with AYVAKIT and for at least two weeks after the final dose of AYVAKIT. Talk to your doctor about the best way to feed your baby during this time.

##### Fertility

AYVAKIT may cause fertility problems in women, and may decrease sperm production in men, which may affect your ability to become pregnant. Consult your doctor if you have any further questions or concerns about fertility.

#### **Driving and using machinery:**

**Do not drive** or operate heavy machinery if you are experiencing cognitive adverse reactions such as confusion or trouble thinking during treatment with AYVAKIT. Also see Side effects section.

#### **Important information about some of this medicine’s ingredients:**

This medicine contains less than 1 mmol sodium (23 mg) per tablet so it is considered sodium free.

### **3. How to use this medicine?**

Always use this medicine according to your doctor’s instructions.

Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine – considering your medical condition and your side effects.

**The usual dose is:** take the prescribed dose one time each day.

#### **Do not exceed the recommended dose.**

#### **How to take this medicine:**

- Take AYVAKIT on an empty stomach at least one hour before or at least two hours after a meal.

There is no information regarding crushing/dividing/chewing of the tablet.

**If you have accidentally taken a higher dose:** if you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

**If you forget to take the medicine,** take the dose as soon as you remember, unless your next scheduled dose is due within 8 hours. Take the next dose at the next regularly scheduled day and time for taking your medicine. Do not take two doses within 8 hours to make up for a forgotten dose.

**If you vomit after taking this medicine,** do not take an extra dose. Take the next dose at the next regularly scheduled day and time for taking your medicine.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

**Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.**

**If you have any further questions about using this medicine, consult your doctor or pharmacist.**

### **4. Side effects**

Like with all medicines, using AYVAKIT may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

#### **Serious side effects:**

##### **AYVAKIT may cause serious side effects, including:**

- **Bleeding in your brain** – this side effect may happen during treatment with AYVAKIT and may sometimes even lead to death. **Stop taking AYVAKIT and tell your doctor**

**right away if you develop any symptoms such as: severe headache, vomiting, drowsiness, dizziness, confusion, slurred speech, or severe weakness on one or both sides of your body.**

If you have AdvSM, your doctor will check your platelet counts before and during treatment with AYVAKIT.

- **Cognitive effects** – cognitive side effects can happen during treatment with AYVAKIT and can even be severe. **Tell your doctor if you notice any new cognitive symptoms or worsening of existing symptoms:**
  - Forgetfulness
  - Confusion
  - Getting lost
  - Trouble thinking
  - Drowsiness
  - Trouble staying awake (somnia)
  - Word finding problems
  - Hallucinations (seeing or hearing things that do not exist in reality)
  - Change in mood or behavior

#### **Other side effects:**

**Very common side effects (may affect more than one in ten users):**

##### **In patients with GIST:**

- Edema (fluid retention) or swelling
- Nausea
- Vomiting
- Tiredness or weakness
- Decreased appetite
- Diarrhea
- Fever
- Shortness of breath
- Accumulation of fluid in the lungs
- Increased eye tearing
- Stomach area (abdominal) pain
- Constipation
- Rash
- Dizziness
- Hair color changes
- Alopecia
- Changes in blood test results (decrease in: hemoglobin, leukocytes, neutrophils, platelets, phosphate, potassium, albumin, magnesium, sodium. Increase in: INR, activated partial thromboplastin time, bilirubin, aspartate aminotransferase, creatinine, alanine aminotransferase, alkaline phosphatase)

- Headache
- Sleep problems
- Changes in the sense of taste
- Weight loss

##### **In patients with AdvSM:**

- Edema (fluid retention) or swelling
- Diarrhea
- Nausea
- Vomiting
- Stomach area (abdominal) pain
- Constipation
- Headaches
- Trouble thinking
- Confusion
- Changes in the sense of taste
- Dizziness
- Joint pain
- Bleeding from the nose
- Tiredness or weakness
- Changes in blood test results (decrease in: platelets, hemoglobin, neutrophils, lymphocytes, calcium, potassium, sodium, albumin, magnesium. Increase in: activated partial thromboplastin time, lymphocytes, bilirubin, aspartate aminotransferase, alkaline phosphatase, creatinine, alanine aminotransferase, potassium)

**Common side effects (may affect up to one in ten users):**

##### **In patients with GIST:**

- Hypertension
- Thyroid problems (hyperthyroid, hypothyroid)
- Hand-foot syndrome (erythrodysesthesia [pain, swelling and blisters in the palms of hands/soles of feet])

##### **In patients with AdvSM:**

- Cardiac failure
- Gastrointestinal hemorrhage
- Large intestine perforations
- Ascites
- Gallstones
- Upper respiratory tract infection
- Urinary tract infection
- Herpes zoster flare-up
- Flushing, hot flashes, hypertension, hypotension
- Insomnia
- Pain in the extremities
- Cough, shortness of breath (dyspnea)

- Rash, alopecia, tingling (pruritus), hair color changes
- Decreased appetite
- Increased eye tearing
- Changes in blood test results (decreased phosphate level)

Your doctor may change your dose, temporarily stop, or permanently stop treatment if you develop certain side effects.

**If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.**

#### **Reporting side effects**

You can report side effects to the Ministry of Health by following the link ‘Reporting Side Effects of Drug Treatment’ on the Ministry of Health home page ([www.health.gov.il](http://www.health.gov.il)) which links to an online form for reporting side effects. You can also use this link:

<https://sideeffects.health.gov.il>

You may also report by email to the registration holder’s patient safety unit at: [drugsafety@neopharmgroup.com](mailto:drugsafety@neopharmgroup.com)

### **5. How to store the medicine?**

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

#### **Storage conditions**

Store below 25°C.

To be used within 60 days after first opening.

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

### **6. Additional information**

**In addition to the active ingredient, this medicine also contains:**

Microcrystalline cellulose PH-101, Microcrystalline cellulose PH-200, Copovidone, Croscarmellose sodium, Magnesium stearate (vegetable source).

Tablet shell contains:

Opadry II White film coating (85F18422): polyvinyl alcohol, titanium dioxide, polyethylene glycol, and talc.

The blue printing ink, used only for AYVAKIT 100 mg, AYVAKIT 200 mg and AYVAKIT 300 mg tablets, contains: Shellac Glaze 45% in ethanol, n-butyl alcohol, FD&C blue 1, isopropyl alcohol, titanium dioxide, black iron oxide, propylene glycol, and ammonium hydroxide.

**What the medicine looks like and contents of the pack:** AYVAKIT 25 mg tablets are round, white and coated, debossed with “BLU” on one side and “25” on the other side.

AYVAKIT 50 mg tablets are round, white and coated, debossed with “BLU” on one side and “50” on the other side.

AYVAKIT 100 mg tablets are round, white and coated, imprinted in blue ink with “BLU” on one side and “100” on the other side.

AYVAKIT 200 mg tablets are round, white and coated, imprinted in blue ink with “BLU” on one side and “200” on the other side.

AYVAKIT 300 mg tablets are round, white and coated, imprinted in blue ink with “BLU” on one side and “300” on the other side.

Tablets packaged in a bottle which includes a desiccant. Package size: 30 tablets.

#### **Registration holder’s name and address:**

Neopharm (Israel) 1996 Ltd., 6 Hashiloach Street, POB 7063, Petah Tikva, 4917001

#### **Manufacturer’s name and address:**

Blueprint Medicines Corporation, Cambridge, MA, USA

**Registration number of the medicine in the Ministry of Health’s National Drug Registry:**

AYVAKIT 300 mg 176-84-36967-99

AYVAKIT 200 mg 176-83-36966-99

AYVAKIT 100 mg 176-82-36965-99

AYVAKIT 50 mg 176-81-36964-99

AYVAKIT 25 mg 176-80-36963-99

Approved in June 2024.

*Avvakit tab PIL vr 01B*