

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

This medicine is dispensed with a doctor's prescription only

## **Vitrakvi 20 mg/mL oral solution**

### **Active ingredient**

Each ml contains 20 mg larotrectinib (as sulfate)

Inactive ingredients and allergens: See section 6 “Additional information” and section 2 “Important information about some of the ingredients of this medicine”.

**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 your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

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

Vitrakvi is a monotherapy intended to treat solid tumours displaying NTRK (neurotrophic tyrosine receptor kinase) gene fusion in adults and children.

Vitrakvi is administered when

- these tumours are locally advanced or have spread to other parts of the body or if a surgery to remove the tumour is likely to cause severe complications, and **in addition**
- there are no satisfactory treatment options.

Before you receive Vitrakvi, your doctor will perform a test to check if you carry the change in the NTRK gene.

### **Therapeutic group:**

Anti-neoplastic and immunomodulatory agents, anti-neoplastic agents, protein kinase inhibitors

### **How Vitrakvi works**

In patients whose cancer is due to an altered NTRK gene, the change in the gene causes the body to make an abnormal protein called TRK fusion protein, which can lead to uncontrolled cell growth and cancer. Vitrakvi blocks the activity of TRK fusion proteins and so may slow or stop the growth of the cancerous tumour. It may also help to shrink the cancerous tumour.

If you have any questions on how Vitrakvi works or why it has been prescribed for you, ask your doctor, pharmacist or nurse.

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

<p><b>Do not use this medicine if:</b></p> <ul style="list-style-type: none"><li>• you are sensitive (allergic) to larotrectinib or any of the other ingredients of this medicine (see section 6).</li><li>• you are pregnant or breastfeeding.</li></ul>
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### **Special warnings about using this medicine**

#### **Tests and follow up**

Vitrakvi can increase the level of the liver enzymes ALT and AST and bilirubin in your blood. Your doctor will perform blood tests before and during treatment to check the levels of ALT, AST and bilirubin and check how well your liver is working.

### **Drug interactions**

**If you are taking or have recently taken other medicines, including non-prescription medications and dietary supplements, tell your doctor or pharmacist.** Particularly if you are taking:

- medicines used to treat fungal or bacterial infections: itraconazole, voriconazole, clarithromycin, telithromycin, troleandomycin.
- a medicine used to treat Cushing’s syndrome: ketoconazole.
- medicines used to treat HIV infection: atazanavir, indinavir, nelfinavir, ritonavir, saquinavir, rifabutin, efavirenz.
- a medicine used to treat depression: nefazodone.
- medicines used to treat epilepsy: phenytoin, carbamazepine, phenobarbital.
- a herbal medicine used to treat depression: St. John’s wort (hypericum).
- a medicine used to treat tuberculosis: rifampicin.
- a medicine used for strong pain relief: alfentanil.
- medicines used to prevent organ rejection after an organ transplant: ciclosporin, sirolimus, tacrolimus.
- a medicine used to treat an abnormal heart rhythm: quinidine.
- medicines used to treat migraines: dihydroergotamine, ergotamine.
- a medicine used to treat long-term pain: fentanyl.
- a medicine used to control involuntary movements or sounds: pimozide.
- a medicine helping to stop smoking: bupropion.
- medicines to reduce blood sugar levels: repaglinide, tolbutamide.
- a medicine that prevents blood clots: warfarin.
- a medicine used to reduce the amount of acid produced in the stomach: omeprazole.
- a medicine used to help control high blood pressure: valsartan.
- a group of medicines used to help reduce cholesterol: statins.
- hormonal medicines used for contraception, see section “Contraception – for men and women” below.

If any of the above apply to you (or if you are not sure), talk to your doctor, pharmacist or nurse.

### **Using this medicine with food and drink**

Do not eat grapefruit or drink grapefruit juice while taking Vitrakvi. The reason for this is that it may increase the amount of Vitrakvi in your body.

### **Pregnancy and breastfeeding**

#### Pregnancy

If you are pregnant, think that you may be pregnant or are planning to become pregnant, ask your doctor or pharmacist for advice before taking this medicine.

Do not use Vitrakvi during pregnancy since the effect of Vitrakvi on the fetus is not known.

#### Breastfeeding

Do not breastfeed while taking this medicine and for 3 days after the last dose. The reason for this is that it is not known if Vitrakvi passes into breast milk.

### **Contraception – for men and women**

You should avoid getting pregnant while taking this medicine.

If you are able to become pregnant, your doctor should perform a pregnancy test before you start treatment.

You must use effective methods of contraception while taking Vitrakvi and for at least 1 month after the last dose, if

- you are able to become pregnant. If you use hormonal contraceptives, you should also use a barrier method, such as a condom.

- you have sex with a woman able to become pregnant.

Consult your doctor about the best method of contraception for you.

### **Driving and using machines**

Vitrakvi may make you feel dizzy or tired. If this happens, do not drive, cycle or use any tools or machines.

### **Important information about some of the ingredients of this medicine**

Vitrakvi oral solution contains 2 mg **sodium benzoate** in 1 ml.

Vitrakvi oral solution contains less than 1 mmol (23 mg) of **sodium** per 5 mL, that is to say essentially ‘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. The usual dosage is generally:

#### **Adults (from 18 years)**

- The recommended dose of Vitrakvi is 100 mg (5 ml), twice a day.
- Your doctor will review your dose and change it as needed.

#### **Children and adolescents**

- Your child’s doctor will determine the right dose for your child based on his height and weight.
- The maximum recommended dose is 100 mg (5 ml), twice a day.
- Your child’s doctor will review the dose and change it as needed.

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

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

- Vitrakvi can be taken with or without food.
- Do not eat grapefruit or drink grapefruit juice while taking this medicine.
- Along with this medicine you need a bottle adapter (28 mm diameter) and a syringe that can be used to give medicines by mouth. Use a 1 ml syringe with 0.1 ml marks for doses lower than 1 ml. Use a 5 ml syringe with 0.2 ml marks for doses of 1 ml or more.
  - Press the bottle cap and turn it anti-clockwise to open the bottle.
  - Insert the bottle adapter into the bottle neck and ensure it is well fixed.
  - Push the plunger fully into the syringe and then insert the syringe in the adapter opening. Turn the bottle upside down.
  - Fill the syringe with a small amount of solution by pulling the plunger down, then push the plunger upwards to remove any large bubbles present in the syringe.
  - Pull the plunger down to the mark equal to the dose in mL prescribed by your doctor.
  - Turn the bottle the right way up and take the syringe out of the adapter.
  - Put the syringe in the mouth, pointing towards the inside of the cheek – this will help you swallow the solution naturally. Slowly press the plunger in.
  - Replace the bottle cap and tightly close the bottle - leave the adapter in the bottle.

If necessary, Vitrakvi may be administered via a nasogastric feeding tube. For details on this, please contact your doctor, pharmacist or nurse.

### **If you have taken too high amount of Vitrakvi**

Talk to your doctor, pharmacist or nurse or go to a hospital immediately. Take the medicine package and this leaflet with you. If a child has accidentally swallowed some of the medicine,

immediately contact a doctor or go to a hospital emergency room and bring the medicine package with you.

### **If you forget to take the medicine**

If you forgot to take the medicine at the scheduled time, do not take a double dose to make up for a forgotten dose or if you vomit after taking this medicine. Take your next dose at the usual time and consult your doctor.

Adhere to the treatment as recommended by the doctor.

### **If you stop taking Vitrakvi**

Do not stop taking this medicine without talking to your doctor first. It is important to take Vitrakvi for the period of time prescribed by your doctor.

If you are not able to take the medicine as your doctor prescribed, talk to your doctor immediately.

**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, pharmacist or nurse.**

### **4. Side effects**

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

You should **immediately contact your doctor** if you experience any of the following **serious side effects**:

- feeling dizzy (very common side effect, may affect more than 1 in 10 users), tingling, feeling numb, or a burning feeling in your hands and feet, difficulty walking normally (common side effect, may affect up to 1 in 10 users). These may be symptoms of **nervous system problems**.

Your doctor may decide to reduce the dose, or pause or stop the treatment.

#### **Additional side effects**

##### **Very common (may affect more than 1 in 10 users):**

- you may look pale and feel your heartbeats; these may be symptoms of low level of red blood cells (anaemia)
- flu like symptoms including fever; these may be symptoms of low level of white blood cells (neutropenia, leukopenia)
- nausea or vomiting
- diarrhoea
- constipation
- muscle pain (myalgia)
- feeling tired (fatigue)
- high level of liver enzymes in blood tests
- weight gain.

##### **Common (may affect up to 1 in 10 users):**

- you may bruise or bleed more easily, which could be symptoms of reduced number of platelets (thrombocytopenia)
- change in the sense of taste (dysgeusia)
- muscle weakness
- high level of “alkaline phosphatase” in blood tests (a very common effect in children).

**Not known** (it is not known how often they occur)

You may experience a combination of tiredness, upper right stomach pain, loss of appetite, nausea or vomiting, yellowing of your skin or eyes, bruising or bleeding more easily, and dark urine. These could be symptoms of liver problems.

**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.**

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/>

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

- Avoid poisoning! To avoid 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 and the bottle. The expiry date refers to the last day of that month.

#### **Storage conditions**

- Store in a refrigerator (2°C - 8°C). Do not freeze. After first opening, use within 10 days and store in a refrigerator (2°C - 8°C).
- Do not use this medicine if the bottle or bottle cap looks damaged or if there has been a leak.
- 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 to protect the environment.

### **6. Additional information**

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

- Purified water
- Hydroxypropyl betadex
- Sucralose
- Sodium citrate
- Sodium benzoate
- Strawberry flavour
- Citric acid

### **What the medicine looks like and contents of the pack:**

A colourless to yellow or orange or red or brownish solution. Each pack contains 2 child-resistant glass bottles containing 50 ml of Vitrakvi solution.

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

Bayer Israel Ltd., 36 Hacharash St., Hod Hasharon 45240.

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

Bayer AG, 51368 Leverkusen, Germany

Revised in December 2023 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 164-39-36176-00