

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Vitrakvi 25 mg

Vitrakvi 100 mg

Capsules

Active ingredient

Each Vitrakvi 25 mg capsule contains 25 mg larotrectinib (as sulfate)

Each Vitrakvi 100 mg capsule contains 100 mg larotrectinib (as sulfate)

Inactive ingredients: See section 6 "Additional information".

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 tumors displaying NTRK (neurotrophic tyrosine receptor kinase) gene fusion in adults and children.

Vitrakvi is administered when

- these tumors are locally advanced or have spread to other parts of the body or if a surgery to remove the tumor 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 tumor. It may also help to shrink the cancerous tumor.

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

Do not use this medicine if:

- you are sensitive (allergic) to larotrectinib or any of the other ingredients of this medicine (see section 6).
- you are pregnant or breastfeeding.

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 level 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.

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 (1 capsule of 100 mg or 4 capsules of 25 mg), 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 (1 capsule of 100 mg or 4 capsules of 25 mg), twice a day.
- Your child's doctor will review the dose and change it as needed.

An oral solution of Vitrakvi is available for patients who cannot swallow the capsules.

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.
- Swallow the Vitrakvi capsules whole with a glass of water. Do not open, chew or crush the capsule as it has a very bitter taste.

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).

Unknown frequency (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) 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

- Do not store the medicine above 30°C.
- Do not use this medicine if you notice that the capsules look damaged.
- 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:

Capsule shell:

- Gelatin
- Titanium dioxide

Printing ink:

- Shellac
- FD&C Blue # 2 Aluminium Lake
- FD&C No 2; Indigo carmine aluminium lake (E 132)
- Titanium dioxide
- Propylene glycol
- Strong Ammonia Solution
- Dimeticone

What the medicine looks like and contents of the pack:

- Vitrakvi 25 mg is marketed as white opaque hard gelatin capsule, with blue printing of BAYER-cross and “25 mg” on the body of the capsule.
- Vitrakvi 100 mg is marketed as white opaque hard gelatin capsule, with blue printing of BAYER-cross and “100 mg” on the body of the capsule.

Each carton box contains 1 child-proof plastic bottle containing 56 hard gelatin capsules.

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 September 2023 according to MOH guidelines.

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

164-40-36177-00 ,164-41-36178-00