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

This medicine is dispensed with a doctor's prescription only

Jakavi® 5 mg	Jakavi® 10 mg	Jakavi® 15 mg	Jakavi® 20 mg
Tablets	**Tablets**	**Tablets**	**Tablets**
Each tablet contains: ruxolitinib phosphate 6.60 mg corresponding to ruxolitinib 5 mg	Each tablet contains: ruxolitinib phosphate 13.20 mg corresponding to ruxolitinib 10 mg	Each tablet contains: ruxolitinib phosphate 19.80 mg corresponding to ruxolitinib 15 mg	Each tablet contains: ruxolitinib phosphate 26.40 mg corresponding to ruxolitinib 20 mg

Inactive ingredients and allergens: see section 2 "Important information about some of the medicine's ingredients", and section 6 "Additional information".
Read the entire leaflet carefully before using this medicine, because it contains information that is important for you.
This leaflet contains concise information about this medicine. If you have any further questions, refer to 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 medical condition is similar to yours.

1. What is the medicine intended for?

Jakavi is used to treat:

- Adult patients with an enlarged spleen or with symptoms related to myelofibrosis, a rare type of blood cancer.
- Adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.
- Adults and children aged 12 years and older with acute or chronic graft-versus-host disease (GvHD), who have inadequate response to corticosteroids or other systemic therapies.

Therapeutic group:
Jakavi belongs to a group of antineoplastic medicines that inhibit protein-kinase.
Enlargement of the spleen is one of the characteristics of myelofibrosis. Myelofibrosis is a disorder of the bone marrow, in which the marrow is replaced by scar tissue. The abnormal marrow can no longer produce enough normal blood cells and as a result the spleen becomes significantly enlarged. By blocking the action of certain enzymes (called Janus Associated Kinases), Jakavi can reduce the size of the spleen in patients with myelofibrosis and relieve symptoms such as fever, night sweats, bone pain and weight loss in patients with myelofibrosis. Jakavi can help reduce the risk of serious blood or vascular complications.
Polycythaemia vera is a disorder of the bone marrow, in which the bone marrow produces too many red blood cells. The blood becomes thicker as a result of the increased red blood cells. Jakavi can relieve the symptoms, reduce spleen size and the volume of red blood cells produced in patients with polycythaemia vera by selectively blocking enzymes called Janus Associated Kinases (JAK1 and JAK2), thus potentially reducing the risk of serious blood or vascular complications.
Graft-versus-host disease (GvHD) is a complication which occurs after transplantation when specific cells (T cells) in the donor's graft (e.g. bone marrow) do not recognise the host cells/organs and attack them. By selectively blocking enzymes called JAK

(JAK1 and JAK2), Jakavi reduces symptoms and signs of the disease (acute and chronic forms), leading to disease improvement and survival of the transplanted cells.
There are two forms of GvHD:
Acute GvHD - usually develops at an early stage soon after the transplantation and can negatively affect skin, liver and gastrointestinal tract.
Chronic GvHD - which develops later, usually weeks to months after the transplantation. Almost any organ can be affected by chronic GvHD.
If you have any questions about how Jakavi works or why this medicine has been prescribed for you, refer to your doctor.

2. Before using the medicine

Follow the doctor's instructions carefully. They may differ from the general information detailed in this leaflet.

Do not use this medicine if:

- You are sensitive (allergic) to ruxolitinib or to any of the other ingredients contained in the medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice.
- You are pregnant or breastfeeding.

If this information applies to you, notify your doctor who will then decide whether you should start treatment with Jakavi.

Special warnings regarding use of the medicine

Before treatment with Jakavi, tell your doctor if one of the following conditions applies to you:

- If you have any infection. It may be necessary to treat your infection before starting treatment with Jakavi. It is important that you tell your doctor if you have ever had tuberculosis or if you have been in close contact with someone who has or has had tuberculosis. Your doctor may perform tests to see if you have tuberculosis or other infections. It is important that you tell your doctor if you have ever had hepatitis B.
- If you have any kidney problems. Your doctor may need to prescribe you a different dose of Jakavi.
- If you have or have ever had any liver problems. Your doctor may need to prescribe a different dose of Jakavi.
- If you are taking other medicines (see section "Drug interactions").
- If you have ever had skin cancer.

During treatment with Jakavi, inform your doctor or pharmacist:

- If you experience unexpected bruising and/or bleeding, unusual tiredness, shortness of breath during exercise or at rest, unusually pale skin, or frequent infections (these are signs of blood disorders).
- If you experience fever, chills or other symptoms of infections.
- If you experience chronic coughing with blood-tinged sputum, fever, night sweats and weight loss (these can be signs of tuberculosis).
- If you have any of the following symptoms or if anyone close to you notices that you have any of these symptoms: confusion or difficulty thinking, loss of balance or difficulty walking, clumsiness, difficulty speaking, decreased strength or weakness

on one side of your body, blurred and/or loss of vision. These may be signs of a serious brain infection and your doctor may suggest further testing and follow-up.
- If you develop painful skin rash with blisters (these are signs of shingles, herpes zoster).
- If you notice skin changes. This may require further observation, as certain types of skin cancer (non-melanoma) have been reported.

Children and adolescents
This medicine is not intended for use by children or adolescents aged below 18 years who have myelofibrosis or polycythaemia vera because the use of Jakavi in this age group has not been studied.
For the treatment of graft-versus-host disease (GvHD), Jakavi can be used in children aged 12 years and older.

Tests and follow-up
Blood tests
Before initiating treatment with Jakavi, your doctor will perform blood tests to determine the best starting dose for you. You will need to have further blood tests during treatment so that your doctor can monitor the amount of blood cells (white cells, red cells and platelets) in your body and assess how you are responding to the treatment and whether Jakavi is having an unwanted effect on these cells. Your doctor may need to adjust the dose or stop treatment. Your doctor will carefully check if you have any signs or symptoms of infection before starting and during treatment with Jakavi. Your doctor will also regularly check the level of lipids (fat) in your blood.

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medications and dietary supplements, tell your doctor or pharmacist. It is particularly important to inform your doctor or pharmacist if you take any of the following medicines containing any of the following active ingredients. Your doctor may need to adjust the Jakavi dose for you.
The following medicines may increase the risk of side effects with Jakavi:
- Some medicines used to treat infections. These include medicines to treat fungal infections (such as ketoconazole, itraconazole, posaconazole, fluconazole and voriconazole), medicines used to treat certain types of bacterial infections (antibiotics such as clarithromycin, telithromycin, ciprofloxacin, or erythromycin), medicines used to treat viral infections, including HIV infection/AIDS (such as amprenavir, atazanavir, indinavir, lopinavir/ritonavir, nelfinavir, ritonavir, saquinavir), medicines to treat hepatitis C (boceprevir, telaprevir).
- Nefazodone, a medicine used to treat depression.
- Mibefradil or diltiazem, medicines to treat hypertension and chronic angina pectoris.
- Cimetidine, a medicine to treat heartburn.

The following medicines or substances may reduce the effectiveness of Jakavi:
- Avasimibe, a medicine to treat heart disease.
- Phenytoin, carbamazepine or phenobarbital and other anti-epileptics used to stop seizures or fits.
- Rifabutin or rifampicin, medicines used to treat tuberculosis.
- St. John’s wort (*Hypericum perforatum*), a herbal product used to treat depression.

Additional medicines:
- Dabigatran, cyclosporin, rosuvastatin or digoxin, whose levels in the blood may increase when they are taken together with Jakavi.

During treatment with Jakavi you should never start treatment with a new medicine without checking first with the doctor who prescribed you Jakavi. This includes prescription medicines, non-prescription medicines and herbal or alternative medicines.

Using Jakavi and food
Take Jakavi tablets by mouth, with or without food, every day at the same time.

Pregnancy and breastfeeding
Do not take Jakavi during pregnancy. Talk to your doctor about how to take appropriate measures to avoid becoming pregnant during treatment with Jakavi.
Do not breastfeed during treatment with Jakavi. Tell your doctor if you are breastfeeding.
If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, consult your doctor or pharmacist before using this medicine.

Driving and using machines
If you experience dizziness after taking Jakavi, do not drive or operate machines.

Important information about some of the medicine's ingredients
Jakavi contains lactose and sodium
Jakavi contains lactose (milk sugar). For further information, see section 6. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
This medicine contains less than 1 mmol (23 mg) sodium per tablet, 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 the dosage and treatment regimen of the medicine.
The dosage and treatment regimen will be determined by your doctor only. Your doctor will always tell you exactly how many Jakavi tablets to take.
The dosage of Jakavi depends on the patient's blood cell count. Your doctor will measure the amount of blood cells in your body and find the best dosage for you, particularly if you have liver or kidney problems.
The usual starting dosage in myelofibrosis is generally 15 mg twice daily or 20 mg twice daily, depending on your blood cell count.
The recommended starting dosage in polycythaemia vera and graft-versus-host disease (GvHD) is 10 mg twice daily.
The maximum dosage is 25 mg twice daily.
During the treatment, your doctor may recommend to lower or increase the dose if the results of blood tests show that this is necessary, if you have problems with your liver or kidneys, or if you also need treatment with certain other medicines.

Do not exceed the recommended dose.

Method of administration
You should take Jakavi every day at the same time, with or without food.
If you receive dialysis, take either one single dose or two separate doses of Jakavi only on dialysis days, after the dialysis has been completed. Your doctor will tell you if you should take one or two doses and how many tablets to take for each dose.

Treatment duration
You should continue taking Jakavi for as long as your doctor tells you to. This is a long-term treatment.
Your doctor will regularly monitor your condition to make sure that the treatment is having the desired effect.
If you have questions about how long to take Jakavi, talk to your doctor or pharmacist.
If you experience certain side effects (e.g. blood disorders), your doctor might need to change the amount of Jakavi you have to take or tell you to stop taking Jakavi for a while.

If you have accidentally taken a higher dosage than that prescribed by the doctor or if a child has accidentally swallowed 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 Jakavi at the designated time, do not take a double dose to make up for the forgotten dose. Take the next dose at the regular time and consult your doctor.
Adhere to the treatment as recommended by your doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting your doctor. If you interrupt your treatment with Jakavi, your symptoms related to myelofibrosis or polycythaemia vera may return. In graft-versus-host disease, a reduction in your dose or stopping your treatment with Jakavi is possible if you respond to treatment, and your doctor will supervise this procedure. Therefore, do not stop taking Jakavi or change the dose without consulting with your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take 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
As with any medicine, using Jakavi may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.
Most of the side effects of Jakavi are mild to moderate and will generally disappear after a few days to a few weeks of treatment.

Tell your doctor immediately if you experience any of the following side effects.
Some are very common – effects that may appear in more than 1 in 10 patients, some are common.

Myelofibrosis and polycythaemia vera:
Some side effects could be serious. Seek medical help immediately prior to taking the next scheduled dose of the medicine if you experience the following serious side effects:
Very common side effects – effects that may appear in more than 1 in 10 patients:

- Any sign of bleeding in the stomach or intestines, such as black or bloodstained stools, or vomiting blood.
- Unexpected bruising and/or bleeding, unusual tiredness, shortness of breath during exercise or at rest, unusually pale skin, or frequent infections (possible symptoms of blood disorders).
- Painful skin rash with blisters (possible symptoms of shingles [herpes zoster]).
- Fever, chills or other symptoms of infections.
- Low level of red blood cells (anaemia), low level of white blood cells (neutropenia) or low level of platelets (thrombocytopenia).

Common side effects – effects that may appear in up to 1 in 10 patients:

- Any sign of bleeding in the brain, such as sudden altered state of consciousness, persistent headaches, numbness, tingling, weakness or paralysis.

Additional side effects
Additional side effects include the effects listed below. If you experience these effects, contact your doctor or pharmacist.
Very common side effects – effects that may appear in more than 1 in 10 patients:

- High level of cholesterol or fat in the blood (hypertriglyceridaemia)
- Abnormal liver function test results
- Dizziness
- Headache
- Urinary tract infections
- Weight gain
- Fever, cough, difficult or painful breathing, wheezing, pain in chest when breathing (possible symptoms of pneumonia)
- High blood pressure, which may also be the cause of dizziness and headache
- Constipation
- High level of lipase in the blood

Common side effects – effects that may appear in up to 1 in 10 patients:

- Reduced number of all three types of blood cells - red blood cells, white blood cells, and platelets (pancytopenia)
- Frequently passing wind (flatulence)

Uncommon side effects – effects that may appear in up to 1 in 100 patients:

- Tuberculosis
- Recurrence of hepatitis B infection (which can cause yellowing of the skin and eyes, dark brown coloured urine, right sided stomach pain, fever and nausea or being sick).

Graft-versus-host disease (GvHD)
Some side effects could be serious. Seek medical help immediately prior to taking the next scheduled dose of the medicine if you experience one of the following serious side effects:
Very common side effects – effects that may appear in more than 1 in 10 patients:

- Fever, pain, redness and/or difficulty breathing (possible symptoms of an infection with the cytomegalovirus (*cytomegalovirus infection*))
- Fever, pain when urinating (possible symptoms of a urinary tract infection)
- Fast heart rate, fever, confusion and rapid breathing (possible symptoms of sepsis, which is a serious condition that occurs in response to an infection that causes widespread inflammation)
- Tiredness, fatigue, pale skin (possible symptoms of anaemia which is caused by low level of red blood cells), frequent infections, fever, chills, sore throat or mouth ulcers due to infections (possible symptoms of neutropenia which is caused by low level of white blood cells), spontaneous bleeding or bruising (possible symptoms of thrombocytopenia which is caused by low levels of platelets)
- Low counts of all three types of blood cells - red blood cells, white blood cells, and platelets (pancytopenia)

Additional side effects
Additional possible side effects include the effects listed below. If you experience these side effects, talk to your doctor or pharmacist.
Very common side effects – effects that may appear in more than 1 in 10 patients:

- High levels of cholesterol (*hypercholesterolaemia*)
- Headaches
- High blood pressure
- High level of lipase in the blood
- Abnormal blood test results, which could indicate possible damage to the pancreas (elevated amylase)
- Nausea
- Abnormal liver function test results
- Increased blood level of enzyme from muscle, potentially indicating muscle damage and/or muscle breakdown (increased blood creatine phosphokinase levels)
- Increased blood level of creatinine, which is usually eliminated by the kidneys into the urine, which may mean that your kidneys are not functioning properly

Common side effects – effects that may appear in up to 1 in 10 patients:

- Fever, pain, redness, and/or difficulty breathing (possible symptoms of infection with BK virus)
- Weight gain
- Constipation

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

Side effects can be reported to the Ministry of Health by clicking on the link
'Reporting Side Effects of Drug Treatment' found on the Ministry of Health home

page (www.health.gov.il) which directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. How should the medicine be stored?

Prevent poisoning! To prevent poisoning, this medicine, and any other medicine must be kept 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 appears on the package or blister. The expiry date refers to the last day of that month.
Storage conditions:
Do not store above 25°C.
Do not throw away medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines that you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, the medicine also contains:
Lactose monohydrate, microcrystalline cellulose, sodium starch glycolate (Type A), hydroxypropylcellulose, povidone, silica colloidal anhydrous, magnesium stearate.

Each 5 mg Jakavi tablet contains 71.45 mg of lactose monohydrate.
Each 10 mg Jakavi tablet contains 142.90 mg of lactose monohydrate.
Each 15 mg Jakavi tablet contains 214.35 mg of lactose monohydrate.
Each 20 mg Jakavi tablet contains 285.80 mg of lactose monohydrate.

What the medicine looks like and what are the contents of the package:
Jakavi 5 mg: Round, curved white to almost white tablets with “NVR” debossed on one side and “L5” debossed on the other side.
Jakavi 10 mg: Round, curved white to almost white tablets with “NVR” debossed on one side and “L10” debossed on the other side.
Jakavi 15 mg: Ovaloid, curved white to almost white tablets with “NVR” debossed on one side and “L15” debossed on the other side.
Jakavi 20 mg: Elongated, curved white to almost white tablets with “NVR” debossed on one side and “L20” debossed on the other side.

Pack size:
Each package contains 56 tablets in blister packs.

Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Revised in November 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Jakavi 5 mg: 149 85 33747
Jakavi 10 mg: 158 58 34859
Jakavi 15 mg: 149 86 33748
Jakavi 20 mg: 149 87 33750