Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Xeljanz® 5 mg

Active ingredient
Each tablet contains tofacitinib 5 mg

Inactive ingredients and allergens: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.
Read the entire leaflet carefully before 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 medical condition is similar to yours.
This medicine is intended for adults over the age of 18.

In addition to the patient information leaflet, Xeljanz 5 mg also has a patient safety information card for ulcerative colitis patient. This card contains important safety information that you need to know and that you should follow before you start and during treatment with Xeljanz 5 mg. Carefully read the patient safety information card and patient information leaflet before using this medicine. Keep the card in case you need to read it again.

Product-specific information:
1. Serious infections: This medicine affects your immune system and can lower the ability of your immune system to fight infections. Some people can have serious infections while taking this medicine, including tuberculosis, and infections caused by bacteria, fungi, or viruses that can spread throughout the body. Some patients have died from these infections. You may be at a higher risk of developing shingles (herpes zoster). Patients with ulcerative colitis taking the higher dose of Xeljanz (10 mg twice daily) have a higher risk of developing serious infections and shingles.
2. Increased risk of death in patients who are 50 years of age and older, have at least one heart disease (cardiovascular) risk factor, and are taking Xeljanz 5 mg, twice daily or 10 mg twice daily.
3. Cancer and immune system problems:

- This medicine may increase your risk of getting cancer because it affects your immune system. Lymphoma and other cancers including skin cancer can develop after taking this medicine. Patients taking Xeljanz 5 mg twice daily or 10 mg twice daily have a higher risk of getting certain cancers including lymphoma and lung cancer, especially if you are a current or past smoker. Patients with ulcerative colitis taking the higher dose of Xeljanz (10 mg twice daily) have a higher risk of skin cancer.
- Some patients who have taken Xeljanz with other medicines that are used to prevent kidney transplant rejection have had a problem with certain white blood cells growing

out of control (Epstein Barr Virus-associated post-transplant lymphoproliferative disorder).

4. **Increased risk of major cardiovascular events such as heart attack, stroke or death in patients 50 years of age and older who have at least one heart disease (cardiovascular) risk factor and are taking Xeljanz 5 mg twice daily or 10 mg twice daily, especially if you are a current or past smoker** .
   Get emergency help right away if you have any symptoms of a heart attack or stroke while taking Xeljanz, including:
   - discomfort in the center of your chest that lasts for more than a few minutes, or that goes away and comes back.
   - severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw.
   - pain or discomfort in your arms, back, neck, jaw, or stomach.
   - shortness of breath with or without chest discomfort.
   - breaking out in a cold sweat.
   - nausea or vomiting.
   - feeling lightheaded.
   - weakness in one part or on one side of your body.
   - slurred speech.
5. **Blood clots in the lungs, veins of the legs or arms, and arteries.** Blood clots in the lungs (pulmonary embolism), veins of the legs (deep vein thrombosis) and arteries (arterial thrombosis) have happened more often in patients who are 50 years of age and older and with at least one heart disease (cardiovascular) risk factor taking Xeljanz 5 mg twice daily or 10 mg twice daily. Blood clots in the lungs have also happened in patients with ulcerative colitis. Some patients have died from these blood clots.
   - Stop taking Xeljanz and tell your doctor right away if you develop signs and symptoms of blood clot, such as sudden shortness of breath or difficulty breathing, chest pain, swelling of the arm or leg, leg pain or tenderness, or redness or discoloration in the arm or leg.
6. **Tears (perforations) in the stomach or intestines:** Patients taking this medicine can get tears in their stomach or intestines. This mainly happens if they also take nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or methotrexate.
7. **Allergic reactions:** Symptoms such as swelling of your lips, tongue, or throat, or hives (raised, red patches of skin that are often very itchy) that may mean you are having an allergic reaction have been seen in patients taking Xeljanz. Some of these reactions were serious. If any of these symptoms occur while you are taking Xeljanz, stop taking the medicine and call your doctor right away.
8. **Changes in blood test results:** Certain blood test results may change because you are using this medicine. Your doctor will make sure you do blood tests (including liver function tests) before you start and while you are using this medicine. Your doctor will make sure your cholesterol level is checked 4 to 8 weeks after you start this medicine and again later, if necessary. Normal cholesterol levels are important to your health.
   Your doctor may stop your medicine for a period of time if needed because of changes in your blood test results.
   You should not receive Xeljanz if your lymphocyte level, neutrophil level, or red blood cell level is too low or the measures of your liver function are too high.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Xeljanz is intended for:

- treatment of adults over the age of 18 with moderate to severe rheumatoid arthritis in whom methotrexate treatment did not work well or could not be tolerated. The medicine

can be used as monotherapy or in combination with methotrexate or any other nonbiologic DMARD (disease-modifying antirheumatic drugs).

- treatment of adults over the age of 18 with active psoriatic arthritis in which methotrexate or another DMARD (disease-modifying antirheumatic drugs) did not work well or could not be tolerated.

- treatment of adults over the age of 18 with moderate to severe active ulcerative colitis when earlier conventional or biologic therapy did not work well, could not be tolerated or response was lost.

Therapeutic group: Janus kinase (JAK) inhibitor.

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).

Special warnings regarding use of the medicine

Before treatment with Xeljanz, tell your doctor if:

- you think you have any kind of infection, tend to get infections, or if you have infections that keep coming back.
- you have symptoms of infection such as fever, sweating, chills, muscle aches, cough, shortness of breath, blood in phlegm, weight loss, red and/or warm and/or painful skin, sores on your skin, diarrhea, stomach pain, burning when you urinate, urinating more often than normal, feeling tired.
- you are taking medicines for an infection.
- you have diabetes, chronic lung disease, HIV, or you have a weak immune system. Patients with these conditions have a higher chance for infections.
- you have tuberculosis or have been in close contact with someone with tuberculosis.
- you have visited, have lived or live in a country or region where there is an increased chance for getting certain kinds of fungal infections (such as histoplasmosis, coccidioidomycosis, or blastomycosis). These infections may happen or become more severe if you are taking this medicine. Consult your doctor if you do not know if you have lived in an area where these infections are common.
- you have or had hepatitis B or hepatitis C. It is not known if this medicine is effective and safe to use in patients who have hepatitis B or C.
- Tell your doctor right away if after starting this medicine you have an infection or symptoms of an infection. This medicine may make you get an infection or make worse any infection that you have.
- you are a current or past smoker.
- you have had any type of cancer.
- you have had a heart attack, other heart problems or stroke.
- you have had blood clots in the veins of your legs, arms, or lungs, or clots in the arteries in the past.
- you have impaired liver or kidney function.
- you have stomach area pain or have been diagnosed with diverticulitis (inflammation of the large intestine), perforations in your digestive system, or an ulcer in your stomach or intestines.

- you have fever and/or stomach pain that does not go away or a change in your bowel habits.
- Tell your doctor if you have recently received or are scheduled to receive a vaccine soon. You should not receive a live vaccine while you are taking this medicine. You can receive non-live vaccines.

Tests and follow-up
- Your doctor will refer you for tuberculosis testing before starting and during treatment.
- Your doctor will monitor you for signs and symptoms of tuberculosis during treatment.
- Your doctor will make sure you do blood tests (including liver function tests) before you start and while you are taking this medicine.
- Your doctor will make sure to check your cholesterol level 4 to 8 weeks after you start treatment, and as needed after that.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
- other medicines to treat rheumatoid arthritis, psoriatic arthritis, or ulcerative colitis. While you are taking Xeljanz, do not take tocilizumab, etanercept, adalimumab, infliximab, rituximab, abatacept, anakinra, certolizumab, golimumab, ustekinumab, secukinumab, azathioprine, vedolizumab, cyclosporine, or any other immunosuppressive drug. The combination may increase your risk of infection.
- medicines that affect the way liver enzymes work. Consult your doctor if you are not sure if medicines you are taking belong to this group.
- if you have recently received or are scheduled to receive a vaccine soon.
- if you are taking medicines to prevent kidney transplant rejection. The combination can cause an increase in the level of white blood cells (Epstein-Barr Virus-associated post-transplant lymphoproliferative disorder).

Using this medicine and food
You can take this medicine with or without a meal.

Pregnancy and breastfeeding
Tell your doctor if you are pregnant or plan to become pregnant while you are taking this treatment. Xeljanz can affect the ability of women to get pregnant. It is not known if this condition is reversible once Xeljanz is stopped. It is not known if Xeljanz will harm an unborn baby.
If you are breastfeeding or plan to breastfeed: You and your doctor should decide if you will either breastfeed or take Xeljanz, but not both at the same time. After you stop your treatment with Xeljanz do not start breastfeeding again until 18 hours after your last dose of Xeljanz.

Important information about some of this medicine's ingredients
This medicine contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to certain sugars, consult your doctor before starting treatment with this medicine.
This medicine contains less than 1 millimole sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this preparation according to your doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined by your doctor only.
Your doctor may reduce your dosage depending on your medical condition.
Do not exceed the recommended dose.
Taking this medicine: Swallow the medicine whole and intact with a glass of water. There is no information about crushing/splitting/chewing.
There is no information about using Xeljanz as monotherapy to treat psoriatic arthritis. Will be given in combination with other medicines as instructed by the doctor.

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 at the scheduled time, do not take a double dose. Take the next dose at the usual time and consult your doctor.

Adhere to the treatment as recommended by your doctor.

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

Do not take medicines in the dark! Check the label and dose <u>each 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, use of Xeljanz, may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Activation of type B or C viral liver infection (hepatitis) in patients who carry the virus in their blood. If you are a carrier of the hepatitis B or C virus (viruses that affect the liver), the virus may become active while you are taking this medicine. Your doctor may refer you for blood tests before you start treatment and while you are taking it.
Consult your doctor if:

- **you have any of the following side effects which could be a symptom of a hepatitis B or C infection:** feel tired, skin or eyes are yellow, little or no appetite, vomiting, change in color of bowel movements (clay-colored bowel movements) fever, chills, stomach discomfort, muscle aches, dark urine, rash.

- Changes in certain blood test results: changes in lymphocyte levels (white blood cells that help fight off infections), low neutrophil level (neutrophils are white blood cells that help fight off infections), low red blood cell level – a sign of anemia, which may make you feel tired and weak.

Side effects in rheumatoid arthritis patients and psoriatic arthritis patients who take Xeljanz include:
Common side effects: upper respiratory tract infections (sinus infection, common cold), headache, diarrhea, nasal congestion, sore throat, runny nose (nasopharyngitis), high blood pressure.

Additional side effects: cough, anemia, vomiting, abdominal pain, diverticulitis, dehydration, insomnia, paresthesia, shortness of breath, congested sinus, interstitial lung disease, dyspepsia, gastritis, nausea, fatty liver, rash, erythema (skin redness), itching, musculoskeletal pain, joint pain, tendonitis, joint swelling, non-melanoma skin cancer, fever, fatigue, peripheral edema.

Common side effects in ulcerative colitis patients taking Xeljanz include: nasal congestion, sore throat, runny nose (nasopharyngitis), increased cholesterol levels, headache, upper respiratory tract infection (common cold, sinus infection), increased levels of creatine phosphokinase, rash, diarrhea, shingles (herpes zoster).

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 or by using the link:
https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning. 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. Shelf-life after first opening: 30 days for 28 and 60 tablet packs, 135 days for 180 tablet packs.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:
microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, and Opadry II White 33G28523.
The Opadry II White 33G28523 film-coating contains:
lactose monohydrate, HPMC 2910 / hypromellose 6cP, titanium dioxide, macrogol/PEG3350 and triacetin (glycerol triacetate).

What the medicine looks like and contents of the pack:
Xeljanz 5 mg: a round, film-coated, white tablet with the word "Pfizer" imprinted on one side and "JKI 5" on the other side.
Each bottle contains 28, 60, or 180 tablets.

Not all pack sizes may be marketed.

Registration holder and address: Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725

Registration number of the medicine in the Ministry of Health's National Drug Registry: 152.35.33973
Revised in 02/2022 according to MOH guidelines.