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PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Xeljanz® 5 mg

Each tablet contains Tofacitinib 5 mg

Inactive and allergenic ingredients in the preparation - in section 6.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

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

This medicine is intended for adults over the age of 18.

In addition to the leaflet, the Xeljanz® 5 mg preparation comes with a Safety Information Card for patients with ulcerative colitis. This card includes important safety information that you should be aware of, and adhere to, before starting and during treatment with Xeljanz® 5 mg. Read the Patient Safety Information Card and the Patient Leaflet before starting to use the preparation. Keep the card for further review, if necessary.

SPECIFIC INFORMATION FOR THE PREPARATION:

Infections: This medicine affects the immune system and can lower the ability of the immune system to fight infections. Some patients can suffer from serious infections while taking the medicine, including tuberculosis or infections caused by bacteria, fungi, or viruses that may spread throughout the body. Some patients have died from these infections.

You may be at a higher risk of developing shingles (herpes zoster). Patients taking the higher dosage (10 mg twice daily) of Xeljanz® have a higher risk of developing serious infections and shingles.

Cancer and immune system problems:

1. The medicine may increase the risk of developing cancer, since it affects the immune system. Lymphoma and other types of cancer, including skin cancer, can develop as a result of taking the medicine. Patients taking the higher dosage (10 mg twice daily) of Xeljanz® have a higher risk of skin cancers.
2. Some patients who took Xeljanz® concomitantly with other medicines to prevent kidney transplant rejection, developed a problem with certain white blood cells whose levels rose uncontrollably.

Tears (perforations) in the stomach or intestines: Patients taking this medicine may suffer from tears in the stomach or intestines, primarily if they are taking nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or methotrexate.

Allergic reactions: Symptoms such as swelling of your lips, tongue or throat, or hives (raised, red patches on the skin that are sometimes very itchy) that may indicate that you are having an allergic reaction, have been seen in patients taking Xeljanz®. Some of these reactions are very serious. If any of these symptoms occur while you are taking Xeljanz®, stop taking Xeljanz® and refer to your doctor right away.

Change in blood test results: Some blood test results may change due to use of the medicine. The attending doctor will make sure to have blood tests performed (including a liver function test) before using and during use of the medicine. The attending doctor will make sure to check cholesterol levels 4 to 8 weeks after commencement of treatment with the medicine, and afterwards, as needed. A normal cholesterol level is important for your health.

The attending doctor may discontinue the medicine for some time, if necessary, if changes in blood test results occur.

You should not take Xeljanz® if the lymphocyte, neutrophil or red blood cell levels are too low or if the parameters indicating liver functions are too high.

1. WHAT IS THE MEDICINE INTENDED FOR?

Xeljanz® is intended for:

- treatment of moderate to severe rheumatoid arthritis in adults over the age of 18 in whom methotrexate therapy was not effective or tolerated. The medicine can be taken as a monotherapy or in combination with methotrexate or any other DMARD (Disease Modifying Antirheumatic Drugs) that is not a biological DMARD.
- treatment of active psoriatic arthritis, in adults over the age of 18, in whom methotrexate therapy or another DMARD (Disease Modifying Antirheumatic Drugs) was not effective or tolerated.
- treatment of moderately to severely active ulcerative colitis in adults over the age of 18 when previous conventional or biological treatment was not effective, not tolerated or the response was lost.

Therapeutic group: a medicine from the Janus kinase (JAK) enzyme inhibitors group.

2. BEFORE USING THE MEDICINE

☒ Do not use the medicine if:

x you are sensitive (allergic) to the active ingredient or to any of the other ingredients contained in the medicine.

Special warnings regarding the use of the medicine:

❗ Before treatment with Xeljanz®, tell the doctor if:

- You think you are suffering from any kind of infection, you have a tendency to develop infections or suffer from recurrent infections.
- You experience symptoms of infection such as: fever, sweating, chills, muscle pain, cough, shortness of breath, blood in the phlegm, weight loss, red and/or hot and/or painful skin, sores on the skin, diarrhea, abdominal pain, burning when passing urine, frequent urination, tiredness.
- You are taking medicines to treat infections.
- You have diabetes, chronic lung disease, AIDS, or have a weak immune system – such patients are at higher risk of suffering from infection.
- You have tuberculosis, or have been in close contact with someone who has tuberculosis.
- You visited, lived or live in a country or region in which there is a higher chance of contracting a fungal infection (e.g., histoplasmosis, coccidioidomycosis or blastomycosis). These infections may be more severe if you are taking the medicine. Consult the doctor if you visited or lived in another country and do not know if these infections are common there.
- You are suffering, or have suffered in the past, from impaired liver or kidney function.
- You have, or have had in the past, hepatitis B or C. It is not known if the medicine is effective and safe in patients with hepatitis B or C.
- Inform the doctor immediately if after commencing treatment with the medicine, you experience an infection or symptoms of an infection. The medicine may cause you to suffer from an infection or worsen the infection from which you are suffering.
- You have cancer.
- You are suffering, or have suffered in the past, from diverticulitis, from tears in the digestive system or from a gastric or intestinal ulcer.
- You are suffering from fever and/or abdominal pain that does not go away or from a change in bowel movement habits.
- Inform the doctor if you have recently received or are scheduled to receive a vaccination; do not receive live vaccines during the treatment with the medicine. Inactivated vaccines can be administered.

❗ If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Especially if you are taking:

- Other medicines to treat rheumatoid arthritis, psoriatic arthritis or ulcerative colitis.

  Tocilizumab, etanercept, adalimumab, infliximab, rituximab, abatacept, anakinra, certolizumab, golimumab, ustekinumab, secukinumab, azathioprine, vedolizumab, cyclosporine, or any other medicine that suppresses the immune system. It is recommended not to take these medicines when taking Xeljanz®. The combination may increase your chance of having an infection.
- A medicine that affects liver enzyme function. If you are not sure whether the medicines you are taking belong to this group, consult the doctor.
- If you have recently received or are scheduled to receive a vaccination.
- If you are taking medicines to prevent rejection of a kidney transplant. The combination may cause an increase in levels of white blood cells (Epstein-Barr Virus-associated post-transplant lymphoproliferative disorder).

❗ Use of the medicine and food

Can be taken with or without a meal.

❗ Pregnancy and breastfeeding

Inform the doctor if you are pregnant or plan to become pregnant during the treatment. Xeljanz® can affect the ability of women to become pregnant. It is not known whether this condition is reversible after stopping Xeljanz®. It is not known whether Xeljanz® may harm the unborn baby.

If you are breastfeeding or plan to breastfeed: decide together with the doctor whether to breastfeed or to take Xeljanz®, but not both together. After stopping treatment with Xeljanz®, do not start breastfeeding until 18 hours after your last dose of Xeljanz®.

❗ Important information regarding some of the ingredients of the medicine

The preparation contains lactose and sodium.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

The doctor can lower the dosage in accordance with your medical condition.

Do not exceed the recommended dose.

- How to take: swallow the medicine whole with a glass of water. There is no information regarding crushing/halving/chewing.
- There is no information regarding treatment with Xeljanz® as a monotherapy for treatment of psoriatic arthritis; it will be given in combination with other medicines in accordance with the doctor's instructions.

Tests and follow up

The doctor will refer you to be tested for tuberculosis before starting and during treatment.

During the treatment with the medicine, the doctor will monitor for signs and symptoms of tuberculosis.

The attending doctor will make sure to have blood tests performed (that include a liver function test) before using and during the use of the medicine.

The attending doctor will make sure to check cholesterol levels 4 to 8 weeks after commencement of treatment with the medicine and afterwards, as needed.

If you took an overdose, or if a child accidentally swallowed the medicine, immediately refer to a doctor or to a hospital emergency room and bring the package of the medicine with you.

If you forget to take this medicine at the required time, do not take a double dose. Take the next dose at the regular time and consult the doctor.

Persist with the treatment as recommended by the doctor.

Even if there is an improvement in your medical condition, do not discontinue treatment with the medicine without consulting the doctor or pharmacist.

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

If you have further questions regarding the use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Xeljanz® 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.

Hepatitis B or C activation: the virus can be activated in patients who carry the virus in their blood if they are taking the medicine. Your doctor may send you for blood tests before and during treatment.

Refer to the doctor immediately if you are suffering from: tiredness, yellow skin or eyes, reduced appetite or complete lack of appetite, vomiting, change in color of stools (clay-colored bowel movements), fever, chills, abdominal discomfort, muscle pain, dark urine, skin rash.

Change in blood test results: change in level of lymphocytes in the blood (white blood cells that help protect against infections), decreased level of neutrophils (white blood cells that help protect against infections), decreased level of red blood cells - a sign of anemia, which may cause tiredness and weakness.

Side effects in rheumatoid arthritis patients and psoriatic arthritis patients taking Xeljanz® include:

Common side effects: upper respiratory tract infection (sinus infection, common cold), headache, diarrhea, nasal congestion, sore throat, runny nose, hypertension.

Additional side effects: cough, anemia, vomiting, abdominal pain, diverticulitis, dehydration, insomnia, numbness, shortness of breath, sinus congestion, interstitial lung disease, indigestion, gastritis, nausea, fatty liver, rash, erythema (reddening of the skin), itchiness, musculoskeletal pain, joint pain, tendonitis, swelling in the joints, 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 infections), increased creatine phosphokinase levels, rash, diarrhea, shingles (herpes zoster).

If a side effect has appeared, if one of the side effects gets worse or when you suffer from a side effect not mentioned in the leaflet, you should consult the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid 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 to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store below 25°C.
- Shelf life after first opening: 30 days for packs of 28 and 60 tablets, 135 days for packs of 180 tablets.

6. FURTHER INFORMATION

- In addition to the active ingredient, the 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).
  A Xeljanz® 5 mg tablet contains lactose.
- **What does the medicine look like and what is the content of the package:**
  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 Street, Herzliya Pituach 46725.
- **Manufacturer name and address:** Pfizer, Freiburg, Germany.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 152.35.33973