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

XELJANZ® 5 mg, tablets
XELJANZ® 10 mg, tablets
XELJANZ® XR 11 mg, extended release tablets

Active ingredient
XELJANZ 5 mg: Each tablet contains tofacitinib 5 mg
XELJANZ 10 mg: Each tablet contains tofacitinib 10 mg
XELJANZ XR 11 mg: Each tablet contains tofacitinib (as citrate) 11 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.

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

1. WHAT IS THIS MEDICINE INTENDED FOR?
XELJANZ is intended for:
- rheumatoid arthritis
- psoriatic arthritis
- ankylosing spondylitis
- ulcerative colitis
- active polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis

Therapeutic group: A Janus kinase (JAK) inhibitor.

Rheumatoid arthritis
XELJANZ is used to treat adult patients with moderate to severe active rheumatoid arthritis, a long-term disease that mainly causes pain and swelling of your joints.

XELJANZ is used together with methotrexate when previous rheumatoid arthritis treatment was not sufficiently effective or was not tolerated. XELJANZ can also be taken on its own in those cases where methotrexate treatment is not tolerated or treatment with methotrexate is not advised.

Treatment with XELJANZ has been shown to reduce pain and swelling of the joints and improve the ability to perform daily activities, when given on its own or together with methotrexate.

Psoriatic arthritis
XELJANZ is used to treat adults with psoriatic arthritis. This is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis, you will first be treated with another medicine. If you do not respond well enough or the medicine is not

tolerated, you may be given XELJANZ to reduce the signs and symptoms of psoriatic arthritis and improve your ability to perform daily activities.

XELJANZ is used together with methotrexate to treat adult patients with active psoriatic arthritis.

Ankylosing spondylitis
XELJANZ is used to treat a condition called ankylosing spondylitis. This condition is an inflammatory disease of the spine.

If you have ankylosing spondylitis, you may first be given other medicines. If you do not respond well enough to these medicines, you will be given XELJANZ. XELJANZ can help to reduce back pain, and improve physical function. These effects can ease your normal daily activities and so improve your quality of life.

Ulcerative colitis
Ulcerative colitis is an inflammatory disease of the large bowel. XELJANZ is used in adult patients to reduce the signs and symptoms of ulcerative colitis when you did not respond well enough or were intolerant to previous treatment.

Active Polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis
XELJANZ is used for the treatment of active polyarticular juvenile idiopathic arthritis a long-term disease that mainly causes pain and swelling of your joints, in patients 2 years of age and older.

XELJANZ is also used for the treatment of juvenile psoriatic arthritis, a condition that is an inflammatory disease of the joints often accompanied by psoriasis, in patients 2 years of age and older.

XELJANZ can be used together with methotrexate when previous treatment for polyarticular juvenile idiopathic arthritis or juvenile psoriatic arthritis was not sufficient or was not well tolerated. XELJANZ can also be taken on its own in those cases where methotrexate treatment is not tolerated or treatment with methotrexate is not advised.

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)
- you have a severe infection such as bloodstream infection or active tuberculosis
- you have been informed that you have severe liver problems, including cirrhosis (scarring of the liver)
- you are pregnant or breast-feeding

If you are not sure regarding any of the information provided above, please contact your doctor.

Special warnings regarding use of the medicine
Before treatment with XELJANZ, tell your doctor if:

- you think you have an infection or have symptoms of an infection such as fever, sweating, chills, muscle aches, cough, shortness of breath, new phlegm or change in phlegm, weight loss, warm or red or painful skin or sores on your skin, difficulty or pain when swallowing, diarrhoea or stomach pain, burning when you urinate or urinating more often than normal, fatigue.
- you have a condition that increases your chance of infection (e.g., diabetes, HIV/AIDS, or a weak immune system).
- you have any kind of infection, are being treated for any infection, or if you have infections that keep coming back. Tell your doctor immediately if you feel unwell.

XELJANZ can reduce your body's ability to respond to infections and may make an existing infection worse or increase the chance of getting a new infection.
- you have or previously had tuberculosis or have been in close contact with someone with tuberculosis. Your doctor will refer you for a tuberculosis test before treatment with XELJANZ and may retest during treatment.
- you have any chronic lung disease.
- you have liver problems.
- you have or previously had hepatitis B or C (viruses that affect the liver). The virus may become active while you are taking XELJANZ. Your doctor may refer you for blood tests for hepatitis before and during use of the medicine.
- you are 65 or older, have ever had any type of cancer, and also if you are a current or past smoker. XELJANZ may increase your risk of certain cancers. White blood cell cancer, lung cancer and other cancers (such as breast, skin, prostate and pancreatic) have been reported in patients treated with XELJANZ. If you develop cancer while taking XELJANZ your doctor will assess whether to stop XELJANZ treatment.
- you are at known risk of fractures, e.g., if you are 65 or older, you are a woman, or take corticosteroids (e.g., prednisone).
- Cases of non-melanoma skin cancer have been observed in patients taking XELJANZ. Your doctor may recommend that you have regular skin examinations while taking XELJANZ. If new skin lesions appear during or after therapy or if existing lesions change appearance, tell your doctor.
- you have had diverticulitis (a type of inflammation of the large intestine) or ulcers in the stomach or intestines (see section 4).
- you have kidney problems.
- you are planning to get vaccinated. Inform your doctor. Certain types of vaccines may not be given when taking XELJANZ. Before starting treatment with XELJANZ, you should receive all the recommended vaccinations. Your doctor will decide whether you need to have a herpes zoster vaccination.
- you have heart problems, high blood pressure, high cholesterol, and also if you are a current or past smoker.

Additionally, before treatment with XELJANZ XR 11 mg, tell your doctor if:
- you have narrowing of the digestive tract as there have been rare cases of blockage in the digestive tract in patients taking other medicines using similar extended-release tablets.
- when you take XELJANZ XR 11 mg, you may sometimes see something in your stool that looks like a tablet. This is the empty shell from the extended-release tablet after the medicine has been absorbed by your body. This is to be expected, and you should not be concerned.

There have been reports of patients treated with XELJANZ who have developed blood clots in the lungs or veins. Your doctor will evaluate your risk to develop blood clots in the lungs or veins and determine if XELJANZ is appropriate for you. If you have already had problems of developing blood clots in lungs and veins or have an increased risk for developing this (for example: if you are seriously overweight, if you have cancer, heart problems, diabetes, experienced a heart attack (within previous 3 months), recent major surgery, if you use hormonal contraceptives/hormonal replacement therapy, if a coagulation defect is identified in you or close relatives), if you are of older age, or if you smoke currently or in the past, your doctor may decide that XELJANZ is not suitable for you.

Contact your doctor straight away if you develop sudden shortness of breath or difficulty breathing, chest pain or pain in upper back, swelling of the leg or arm, leg pain or tenderness, or redness or discolouration in the leg or arm while taking XELJANZ, as these may be signs of a clot in the lungs or veins.

Contact your doctor straight away if you experience acute changes to your eyesight (blurry vision, partial or complete loss of vision), as this may be a sign of blood clots in the eyes.

There have been reports of patients treated with XELJANZ who have had a heart problem, including heart attack. Your doctor will evaluate your risk to develop a heart problem and determine if XELJANZ is appropriate for you. Contact your doctor straight away if you develop signs and symptoms of a heart attack including severe chest pain or tightness (that may spread to arms, jaw, neck, back), shortness of breath, cold sweat, light headedness or sudden dizziness.

Tests and follow-up
Your doctor should refer you for blood tests before you start treatment with XELJANZ, and after 4 to 8 weeks of treatment and then every 3 months, to determine if you have a low white blood cell (neutrophil or lymphocyte) count, or a low red blood cell count (anaemia). Do not take XELJANZ if your white blood cell (neutrophil or lymphocyte) count or red blood cell count is too low. If needed, your doctor may interrupt your XELJANZ treatment to reduce the risk of infection (white blood cell counts) or anaemia (red blood cell counts).
Your doctor may also perform other tests, for example to check your blood cholesterol levels or monitor the health of your liver. Your doctor should test your cholesterol levels 8 weeks after you start taking XELJANZ. Your doctor should perform liver tests periodically.

Elderly
There is a higher rate of infections, some of which may be serious, in patients aged 65 years and older. Contact your doctor as soon as you notice any signs or symptoms of infections. Patients aged 65 years and older may be at increased risk of infections, heart attack and some types of cancer. Your doctor may decide that XELJANZ is not suitable for you.

Asian patients
There is a higher rate of shingles in Japanese and Korean patients. Tell your doctor if you notice any painful blisters on your skin.
You may also be at higher risk of certain lung problems. Contact your doctor if you notice any breathing difficulties.

Children and adolescents
The safety and benefits of XELJANZ have not yet been established in children less than 2 years of age.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

Tell your doctor if you have diabetes or are taking medicines to treat diabetes. Your doctor will decide whether to reduce the anti-diabetic medicine while you are taking XELJANZ.

Some medicines should not be taken with XELJANZ. If these medicines are taken with XELJANZ, they could alter the level of XELJANZ in your body, and the dose of XELJANZ may require adjustment. You should tell your doctor if you are using medicines that contain any of the following active ingredients:
- antibiotics such as rifampicin, used to treat bacterial infections
- fluconazole, ketoconazole, used to treat fungal infections

XELJANZ is not recommended for use with medicines that supress the immune system, including so-called targeted biologic (antibody) therapies, such as those that inhibit tumour necrosis factor, interleukin-17, interleukin-12/interleukin-23, anti-integrins, and strong chemical immunosuppressants, including azathioprine, mercaptopurine, ciclosporin, and tacrolimus. Taking XELJANZ with these medicines may increase your risk of side effects, including infection.
Serious infections and fractures may appear more often in people who also take corticosteroids (e.g., prednisone).

Using this medicine and food
Can be taken with or without a meal.

Pregnancy and breast-feeding
If you are a woman of childbearing age, you should use effective birth control during treatment with XELJANZ and for at least 4 weeks after the last dose.
If you are pregnant or breast-feeding, think you are pregnant or are planning to become pregnant, consult your doctor before taking this medicine. XELJANZ must not be used during pregnancy. Tell your doctor right away if you become pregnant while taking XELJANZ.
If you are taking XELJANZ and breast-feeding, you must stop breast-feeding until you talk to your doctor about stopping treatment with XELJANZ.

Driving and using machines
XELJANZ has no or limited effect on your ability to drive or use machines.

Important information about some of this medicine's ingredients
XELJANZ 5 mg and XELJANZ 10 mg:
The medicine contains lactose monohydrate. If you have been told in the past by your doctor that you have an intolerance to certain sugars, consult your doctor before starting treatment with this medicine.
This medicine contains sodium. This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.
XELJANZ XR 11 mg:
This medicine contains approximately 152 mg sorbitol in each extended-release tablet.

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 uncertain about the dosage and treatment regimen of the medicine.
The dosage and treatment regimen will be determined by your doctor only.

Rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis
The recommended dosage is one 5 mg tablet taken twice a day or one 11 mg extended-release tablet taken once a day.

If you suffer from rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis, your doctor may switch the treatment between XELJANZ 5 mg twice daily and XELJANZ XR 11 mg once daily and vice versa. It is possible to switch treatments on the day following the last dose of either tablet. You should not switch between XELJANZ 5 mg and XELJANZ XR 11 mg unless instructed by your doctor.

Ankylosing spondylitis
Your doctor may decide to stop treatment with XELJANZ if it does not work for you within 16 weeks.

Ulcerative colitis
- The recommended dosage is 10 mg twice a day for 8 weeks, followed by 5 mg twice a day.
- Your doctor may decide to extend the initial 10 mg twice a day treatment by an additional 8 weeks (16 weeks in total), followed by 5 mg twice a day.
- Your doctor may decide to stop XELJANZ if XELJANZ is not effective for you within 16 weeks of treatment.
- For patients, who have previously taken biologic medicines to treat ulcerative colitis (such as those that block the activity of TNF in the body) and these medicines did not work, the doctor may decide to increase your dosage of XELJANZ to 10 mg twice a day if you do not respond sufficiently to 5 mg twice a day. Your doctor will

assess the potential risks, including that of developing blood clots in the lungs or veins, and potential benefits to you. Your doctor will tell you if this applies to you.
- If your treatment is interrupted, your doctor may decide to restart your treatment.

Use in children and adolescents

Polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis
The recommended dose is 5 mg twice a day for patients ≥ 40 kg.

Do not exceed the recommended dose.

How to use:
XELJANZ 5 and 10 mg: Take one tablet in the morning and one tablet in the evening. Try to take the tablets at the same time every day.
The tablets may be crushed and taken with water.
XELJANZ XR 11 mg: Take one tablet a day. Try to take the tablet at the same time every day, e.g., morning or evening.
Swallow the tablet whole in order to ensure the entire dose is actually taken. Do not crush, split, or chew.

Your doctor may reduce the dose if you have liver or kidney problems or if you take certain other medicines. Your doctor may also stop treatment temporarily or permanently if blood tests show low white blood cell or red blood cell counts.

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.
Some of the side effects may be serious and may require medical attention.

Side effects in children and adolescents with active polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis were consistent with those seen in adult rheumatoid arthritis patients with the exception of certain infections (influenza, pharyngitis, sinusitis, viral infection) and gastrointestinal or general disorders (abdominal pain, nausea, vomiting, fever, headache, cough), which were more common in juvenile idiopathic arthritis paediatric population.

Possible serious side effects
In rare cases, infection may be life-threatening.
Lung cancer, white blood cell cancer and heart attack have also been reported.

If you notice any of the following serious side effects you need to tell a doctor straight away.

Signs of serious infections (common) include:
- fever and chills
- cough
- skin blisters
- stomach ache
- persistent headaches

Signs of ulcers or perforations (holes) in your stomach (uncommon) include:
- fever
- stomach or abdominal pain
- blood in the stool
- unexplained changes in bowel movements

Holes in stomach or intestines happen most often in people who also take nonsteroidal anti-inflammatory drugs or corticosteroids (e.g., prednisone).

Signs of allergic reactions (unknown) include
- chest tightness
- wheezing
- severe dizziness or light-headedness
- swelling of the lips, tongue or throat
- hives (itching or skin rash)

Signs of blood clots in lungs or veins or eyes (uncommon: venous thromboembolism) include:
- sudden shortness of breath or trouble breathing
- chest pain or pain in upper back
- swelling of the leg or arm
- leg pain or tenderness
- redness or discolouration in the leg or arm
- acute changes in eyesight

Signs of a heart attack (uncommon) include:
- severe chest pain or tightness (that may spread to arms, jaw, neck, back)
- shortness of breath
- cold sweat
- light headedness or sudden dizziness

Additional side effects

Common side effects (may affect up to 1 in 10 people): lung infection (pneumonia and bronchitis), shingles (herpes zoster), infections of nose, throat or the windpipe (nasopharyngitis), influenza, sinusitis, urinary bladder infection (cystitis), sore throat (pharyngitis), increased muscle enzymes in the blood (sign of muscle problems), stomach pain (which may be from inflammation of the stomach lining), vomiting, diarrhoea, nausea, indigestion, low white blood cell count, low red blood cell count (anaemia), swelling of the feet and hands, headaches, high blood pressure (hypertension), cough, rash, acne.

Uncommon side effects (may affect up to 1 in 100 people): lung cancer, tuberculosis, kidney infection, skin infection, herpes simplex or cold sores (oral herpes), blood creatinine increased (a possible sign of kidney problems), increased cholesterol (including increased LDL), fever, fatigue, weight gain, dehydration, muscle strain, tendonitis, joint swelling, joint sprain, abnormal sensations, poor sleep, sinus congestion, shortness of breath or difficulty breathing, skin redness,

itching, fatty liver, painful inflammation of small pockets in the lining of your intestine (diverticulitis), viral infections, viral infections affecting the gut, some types of skin cancers (non-melanoma-types).

Rare side effects (may affect up to 1 in 1,000 people): blood infection (sepsis), lymphoma (white blood cell cancer), disseminated tuberculosis involving bones and other organs, other unusual infections, joint infections, increased liver enzymes in the blood (sign of liver problems), pain in the muscles and joints.

Very rare side effects (may affect up to 1 in 10,000 people): tuberculosis involving the brain and spinal cord, meningitis, infection of the soft tissue and fascia.
In general, fewer side effects were seen when XELJANZ was used alone than in combination with methotrexate in rheumatoid arthritis.

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
- XELJANZ 5 mg: 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.
- XELJANZ 10 mg: Store below 30°C. Shelf life after first opening: 60 days.
- XELJANZ XR 11 mg: Store below 30°C. Shelf life after first opening: 30 days.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:
XELJANZ 5 and 10 mg:
microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, HPMC 2910 / Hypromellose 6cP, titanium dioxide, macrogol/PEG3350 and triacetin.

XELJANZ 10 mg also contains:
FD&C Blue #2/Indigo Carmine Aluminum Lake (E132)
FD&C Blue #1/Brilliant Blue FCF Aluminum Lake (E133)

XELJANZ XR 11 mg:
sorbitol, hydroxyethyl cellulose, copovidone, cellulose acetate, opadry pink 03k140024 (hpmc 2910/hypromellose, titanium dioxide, triacetin, red iron oxide, purified water), hydroxypropyl cellulose, magnesium stearate, opacode black (shellac glaze in ethanol, isopropyl alcohol, ammonium hydroxide 2, n-butyl alcohol, propylene glycol, ferrosoferric oxide/ black iron oxide), acetone, methanol, purified water, isopropyl alcohol, opadry pink

What the medicine looks like and contents of the pack:
XELJANZ 5 mg:
a round, white, film-coated tablet, with the word "Pfizer" imprinted on one side and "JKI 5" on the other side.
Each bottle contains 28, 60 or 180 tablets.
XELJANZ 10 mg:

a round, blue, film-coated tablet, with the word “Pfizer” imprinted on one side and “JKI 10” on the other side.
Each bottle contains 60 tablets.
XELJANZ XR 11 mg:
an oval, pink tablet, with a drilled hole on the horizontal side and “JKI 11” printed down the length of the tablet.
Each bottle contains 30 tablets.

Not all pack sizes may be marketed.

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

Registration number of the medicine in the Ministry of Health’s National Drug Registry:
XELJANZ 5 mg: 152-35-33973
XELJANZ 10 mg: 170-18-35747
XELJANZ XR 11 mg: 170-19-34983

Revised in 02/2024.