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

XELJANZ® 1 mg/ml, oral solution

Active ingredient
Each ml of solution contains: tofacitinib (as citrate) 1 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 1 mg/ml is indicated for the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive or negative polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis in patients 2 years of age and older, who have responded inadequately to previous therapy with disease modifying antirheumatic drugs (DMARD.)

XELJANZ 1 mg/ml can be given in combination with methotrexate or as monotherapy in case of intolerance to methotrexate treatment or where continued treatment with methotrexate is inappropriate

Therapeutic group: A Janus kinase (JAK) inhibitor.

Active polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis
XELJANZ 1mg/ml 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 1 mg/ml is also used for the treatment of juvenile psoriatic arthritis, an inflammatory disease of the joints often accompanied by psoriasis in patients 2 years of age and older.

XELJANZ 1 mg/ml 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 1 mg/ml 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 (and during) 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 body, difficulty or pain when swallowing, diarrhoea or stomach pain, burning when you urinate or urinating more often than normal, feeling very tired.
- 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. See also 'Do not use this medicine if'.
- 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 have ever had any type of cancer, and/or if you are a current or past smoker. XELJANZ may increase your risk of certain cancers. White blood cell cancer, lung cancer and other types of 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.
- There are known risks of fractures, e.g., in people 65 or older, in women, or in patients who 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 (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 should 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.

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 your close relatives), 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, lightheadedness or sudden dizziness.

Tests and follow-up
Your doctor will test you for tuberculosis before treatment with XELJANZ and may retest during treatment.
Your doctor may refer you for blood tests for hepatitis before and during use of the medicine.
Your doctor may recommend that you have regular skin examinations during treatment with XELJANZ, as cases of non-melanoma skin cancer have been observed in patients taking XELJANZ. Tell your doctor if new skin lesions appear during or after therapy or if existing lesions change appearance.
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
The safety and efficacy of XELJANZ 1 mg/ml has not been established in the elderly. The treatment will be given as decided by the doctor, only if there are no other therapeutic alternatives.

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.

Smoking
If you are a current or past smoker, your doctor may decide that XELJANZ is not suitable for you.

Children and adolescents
XELJANZ 1 mg/ml is not intended for children under 2 years of age.

This medicine contains propylene glycol and should be used with caution in patients 2 years of age and older and only if advised by the doctor (see section: ‘XELJANZ 1 mg/ml contains propylene glycol’).

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 dosage of anti-diabetic medicines 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 contraception 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.
Do not use XELJANZ while breast-feeding. 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 negligible effect on your ability to drive or use machines.

Important information about some of this medicine's ingredients
XELJANZ 1 mg/ml contains propylene glycol
This medicine contains 2.39 mg propylene glycol in each 1 ml of solution.

XELJANZ 1 mg/ml contains sodium benzoate
This medicine contains 0.9 mg sodium benzoate in each 1 ml of solution.

XELJANZ 1 mg/ml contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per ml of solution, 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 the 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.

For detailed instructions for use, see section 'Instructions for Use of XELJANZ 1 mg/ml'.

Use in children 2 years of age and older and adolescents

The recommended dose in patients 2 years of age and older is based upon the following weight categories (see Table 1).

Table 1. XELJANZ dose for patients with polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis two years of age and older

Body weight (kg)	Dose regimen
10 - <20	3.2 mg (3.2 ml of solution) twice daily
20 - <40	4 mg (4 ml of solution) twice daily
≥ 40	5 mg (5 ml of solution or 5 mg tablet) twice daily

Do not exceed the recommended dose.

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 suffer from polyarticular juvenile idiopathic arthritis or juvenile psoriatic arthritis, your doctor may switch you from XELJANZ 5 ml solution twice daily to XELJANZ 5 mg tablets twice daily.

XELJANZ is taken orally. You can take the medicine with or without food.

Try to take the medicine at the same time every day (once in the morning and once in the evening).

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 continue as normal.

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 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 (see also section 'Special warnings regarding use of the medicine')
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 aches
- 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 frequency) include:
- chest tightness
- wheezing
- severe dizziness or lightheadedness
- 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 difficulty 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
- lightheadedness 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
  Do not store above 25°C.
  Store the solution in the original bottle and carton in order to protect from light.
  Shelf life and storage temperature after first opening: 60 days at 25°C.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:

- Purified water, xylitol (E967), grape flavour [propylene glycol (E1520), glycerol (E422), ethanol and other components], lactic acid (E270), sucralose (E955), sodium benzoate (E211), hydrochloric acid.

What the medicine looks like and contents of the pack:
A clear, colourless solution in a white HDPE 250 ml bottle containing 240 ml of solution.
Each pack contains one bottle, one press-in bottle adapter, and one oral dosing syringe with 3.2 ml, 4 ml, and 5 ml graduations.

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:

176-47-37836-99

7. Instructions for Use of XELJANZ 1 mg/ml

Read the Instructions for Use before you start using XELJANZ 1 mg/ml. There may be new information.

Important information about measuring XELJANZ 1 mg/ml

Always use the oral dosing syringe that comes in the package to measure and take the dose prescribed to you. Ask your doctor or pharmacist to show you how to measure the dose prescribed to you if you are not sure.

How to store XELJANZ?

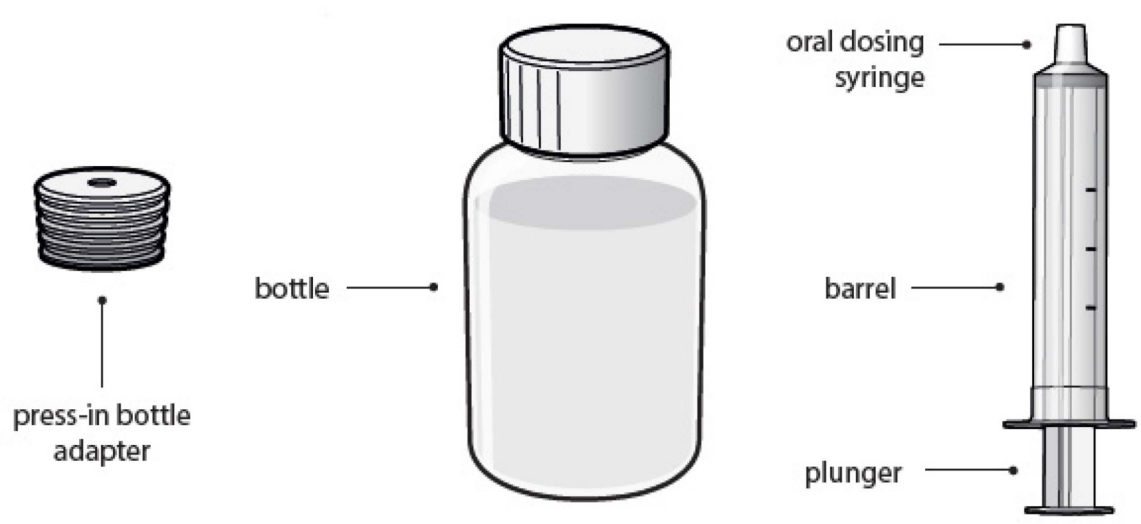
Keep out of the sight and reach of children.

Discard remaining XELJANZ oral solution after 60 days.
To help you remember when to dispose of the XELJANZ bottle, you can write the date the bottle was opened on the carton and here:
Date bottle was opened: ____ / ____ / ____.

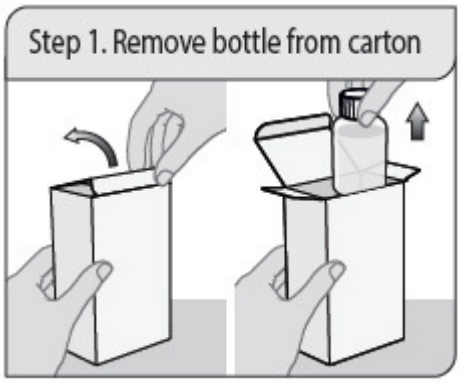
Before each use:
Wash your hands with soap and water and place the contents of the carton on a clean flat surface.

Each carton of XELJANZ 1 mg/ml contains:

- 1 press-in bottle adapter
- 1 bottle of XELJANZ solution
- 1 oral dosing syringe with graduations

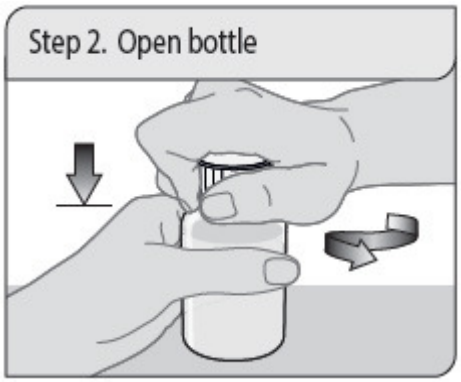


Step 1: Remove bottle from carton



Remove the bottle of XELJANZ 1 mg/ml from the carton.

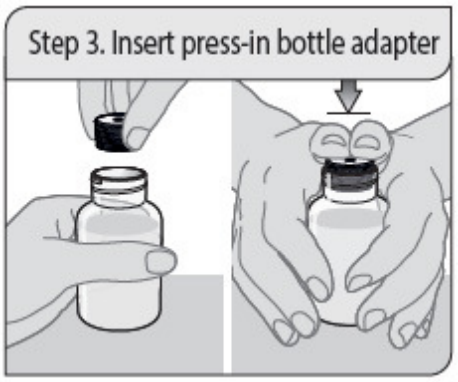
Step 2: Open bottle



Open the bottle. Remove the seal off the top of the bottle (first time only).

Do not throw away the child-resistant cap.
Note: Bottle **does not need** to be shaken before use.

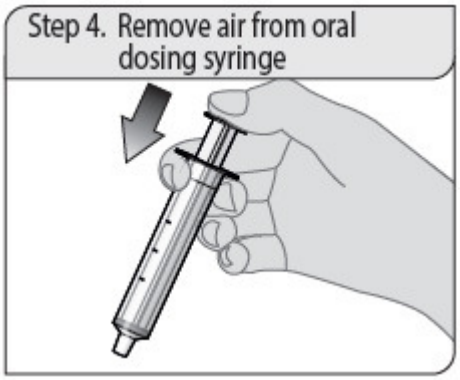
Step 3: Insert press-in bottle adapter



Remove the press-in bottle adapter and oral dosing syringe from the plastic overwrap. Place the bottle on a flat surface. Push the ribbed end of the press-in bottle adapter with your thumbs all the way into the neck of the bottle while holding the bottle firmly.

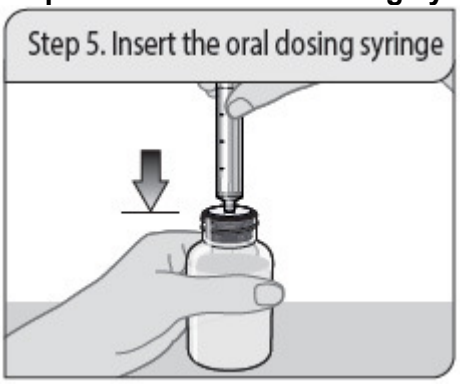
Note: Do not remove the press-in bottle adapter from the bottle after it is inserted.

Step 4: Remove air from oral dosing syringe



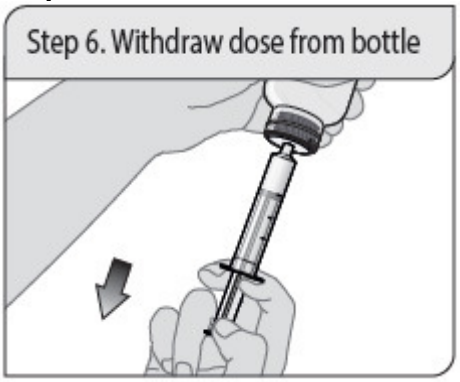
Push the oral dosing syringe plunger fully to the tip of the syringe barrel to remove excess air.

Step 5: Insert the oral dosing syringe



Insert the oral dosing syringe into the upright bottle through the opening of the press-in bottle adapter until the syringe is firmly in place.

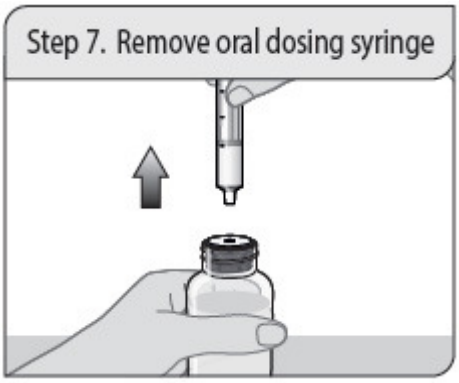
Step 6: Withdraw dose from bottle



With the oral dosing syringe in place, turn the bottle upside down. Pull back the plunger.

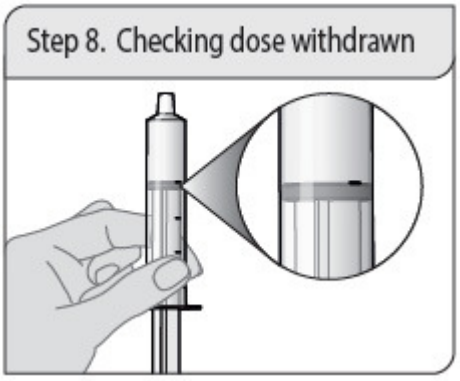
If you see air bubbles in the oral dosing syringe, fully push the plunger in to empty the oral solution back into the bottle. Then withdraw the dose prescribed to you by your doctor.

Step 7: Remove oral dosing syringe



Turn the bottle upright and place the bottle on a flat surface. Remove the oral dosing syringe from the bottle adapter and bottle by pulling straight up on the oral dosing syringe barrel.

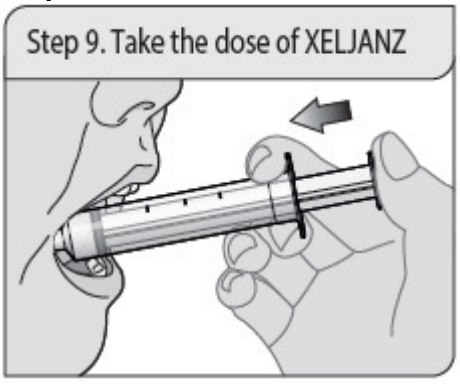
Step 8: Checking dose withdrawn



Check that the correct dose was drawn up into the oral dosing syringe.

If the dose is not correct, insert the oral dosing syringe tip firmly into the bottle adapter. Fully push in the plunger so that the solution flows back into the bottle. Repeat Steps 6 and 7.

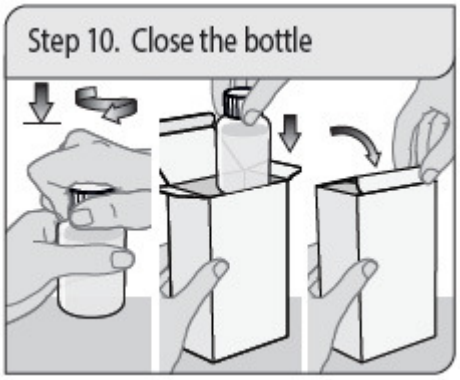
Step 9: Take the dose of XELJANZ



Place the tip of the oral dosing syringe into the inside of the patient's cheek.

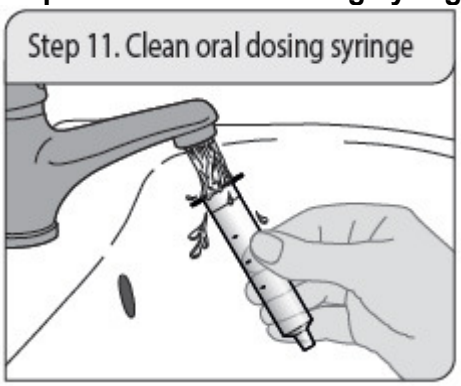
Slowly push the plunger all the way down to give all the medicine in the oral dosing syringe. Make sure the patient has time to swallow the medicine.

Step 10: Close the bottle



Close the bottle tightly by turning the child-resistant cap clockwise, leaving the press-in bottle adapter in place.
Place the bottle back into the carton and close the carton to protect the medicine from light.

Step 11: Clean oral dosing syringe



Remove the plunger from the barrel by pulling the plunger and the barrel away from each other.
Rinse both with water after each use.
Allow both parts of the syringe to air dry; then put the syringe back into the carton that contains the bottle.
Store the oral dosing syringe with the bottle of solution.

Do not throw away the oral dosing syringe.

Revised in 07/2024