

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

This medicine is dispensed with a doctor's prescription only

**SEROQUEL XR® 50 mg
Prolonged-release tablets**

**SEROQUEL XR® 150 mg
Prolonged-release tablets**

**SEROQUEL XR® 200 mg
Prolonged-release tablets**

**SEROQUEL XR® 300 mg
Prolonged-release tablets**

**SEROQUEL XR® 400 mg
Prolonged-release tablets**

The active ingredient and its quantity:

Each tablet of Seroquel XR 50 mg contains:
quetiapine (as fumarate) 50 mg

Each tablet of Seroquel XR 150 mg contains:
quetiapine (as fumarate) 150 mg

Each tablet of Seroquel XR 200 mg contains:
quetiapine (as fumarate) 200 mg

Each tablet of Seroquel XR 300 mg contains:
quetiapine (as fumarate) 300 mg

Each tablet of Seroquel XR 400 mg contains:
quetiapine (as fumarate) 400 mg

Inactive ingredients and allergens in this medicine, please see section 2 – 'Important information about some of this medicine's ingredients' and section 6 - 'Additional information'.

Read the entire leaflet carefully before you start using this medicine.

This leaflet contains concise information about the medicine. If you have 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 illness is similar to yours.

The medicine is not intended for children and adolescents under the age of 18 years.
This medicine is not intended for elderly people who suffer from dementia.

- Antidepressants and anti-anxiety medicines increase the risk of suicidal behavior and thoughts among children, adolescents and young adults up to 25 years of age. When starting treatment with this medicine, patients of all ages and their relatives, must monitor behavioral changes such as

worsening of depression, suicidal thoughts, aggressiveness etc. If changes such as these occur, refer immediately to the doctor.

- Elderly patients who suffer from dementia-related psychosis and are treated with antipsychotics, have an increased risk of death.

1. WHAT IS THIS MEDICINE INTENDED FOR?

- to treat schizophrenia.
- to treat manic episodes associated with bipolar disorders.
- to treat depression associated with bipolar disorders.
- to treat depression together with an additional antidepressant.

Therapeutic group:

Antipsychotics.

2. BEFORE USING THIS MEDICINE

Do not use Seroquel XR if:

- you are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (please see section 6 – ‘Additional information’).
- you are taking any of the following medicines:
 - medicines for treating acquired immune deficiency syndrome (HIV).
 - medicines from the azole family (for treatment of fungal infections).
 - erythromycin or clarithromycin (for treatment of infections).
 - nefazodone (for treatment of depression).

If you are not sure, refer to the doctor or pharmacist before taking Seroquel XR.

Special warnings about using Seroquel XR

Before using Seroquel XR, tell your doctor if:

- you, or someone in your family, have or have had any heart problems such as heart rhythm problems, weakening or inflammation of the heart muscle or if you are taking any medicines that may have an impact on the way your heart beats.
- you have low blood-pressure.
- you have had a stroke, especially if you are elderly.
- you have liver problems.
- you have ever had seizures.
- you have diabetes or have a risk of getting diabetes. If you do, your doctor may check your blood sugar levels while you are taking Seroquel XR.
- you have had a low white blood cell count in the past (which may have been caused by other medicines).
- if you are an elderly person with dementia, do not take Seroquel XR. Seroquel XR may increase the risk of stroke, or in some cases the risk of death, in elderly people with dementia.
- you are an elderly person with Parkinson’s disease/parkinsonism.

- you or a family member have a medical history of blood clots, as medicines of this type are involved in creating blood clots.
- you have or have had: a condition where you stop breathing for short periods during your nightly sleep (called “sleep apnea”) and are taking medicines that slow down the normal activity of the brain.
- you have or have had: a condition where you can’t completely empty your bladder (urinary retention), have an enlarged prostate, a blockage in your intestines, or increased pressure inside your eye. These conditions are sometimes caused by medicines (called “anticholinergics”) that affect the way nerve cells function in order to treat certain medical conditions.
- you have a history of alcohol or drug abuse.
- you have depression or other conditions that are treated with antidepressants. The use of these medicines together with Seroquel XR can lead to serotonin syndrome, a potentially life-threatening disorder (see section 2 “Drug interactions”).

Inform the doctor immediately if you feel any of the following symptoms after taking Seroquel XR:

- A combination of fever, acute muscle stiffness, sweating, or reduced consciousness (this is a phenomenon called “neuroleptic malignant syndrome”). You may need urgent medical treatment.
- Involuntary movements, mainly of the face and tongue.
- Dizziness, a severe sense of feeling sleepy, which can increase the risk of accidental fall in elderly people.
- Fits (seizures).
- Long-lasting and painful erection.
- You have a fast and irregular heartbeat, even when you are at rest, palpitations, breathing problems, chest pain or unexplained tiredness. Your doctor will need to check your heart and if necessary, refer you to a cardiologist immediately.

Inform the doctor as soon as possible if you feel any of the following symptoms after taking Seroquel XR:

- A fever, flu-like symptoms, sore throat, or any other infection, as this could be a result of a very low white blood cell count, which may require Seroquel XR to be stopped and/or treatment to be given.
- Constipation along with persistent abdominal pain, or constipation which has not responded to medicinal treatment, as this may lead to a more serious blockage of the bowel.

Suicidal thoughts and exacerbated depression

If you are depressed, you may sometimes have suicidal thoughts. Increased suicidal thoughts can occur when first starting treatment with Seroquel XR, since it takes time for the medicine to work, usually about two weeks but sometimes longer. These thoughts may also be increased if you suddenly stop the treatment.

These thoughts are more likely in young adults. Information from clinical trials has shown an increased risk of suicidal thoughts and/or suicidal behavior in young adults aged less than 25 years with depression.

If you have suicidal thoughts at any time, contact your doctor or go to a hospital straight away. You may find it helpful to tell a relative or close friend that you are depressed, and ask them to read this leaflet. You might ask them to tell you if they think your depression is getting worse, or if they are worried about changes in your behavior.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) which can be life threatening or fatal are very rare and have been reported in patients taking this medicine. These are commonly manifested by:

- Stevens-Johnson syndrome (SJS) - a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals.
- Toxic Epidermal Necrolysis (TEN), Lyell's syndrome, a more severe form causing extensive peeling of the skin.
- DRESS syndrome - Drug Reaction with Eosinophilia and Systemic Symptoms consists of flu-like symptoms with a rash, fever, swollen glands, and abnormal blood test results (including increased white blood cells (eosinophilia) and increased liver enzymes level).
- Acute Generalized Exanthematous Pustulosis (AGEP) - small blisters filled with pus.
- Erythema Multiforme (EM) - skin rash with itchy-red irregular spots.

Stop using Seroquel XR if you develop these symptoms and contact your doctor or seek medical attention immediately.

Weight gain

Weight gain has been seen in patients taking Seroquel XR. You and your doctor should check your weight regularly.

Children and adolescents

The medicine is not intended for children and adolescents under 18 years of age!

Drug interactions

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

Do not take Seroquel XR if you are taking any of the following medicines:

- medicines for treating acquired immune deficiency syndrome (AIDS).
- Azole medicines (for treatment of fungal infections).
- Erythromycin or clarithromycin (for treatment of infections).
- Nefazodone (for treatment of depression).

Tell your doctor or the pharmacist if you are taking:

- medicines for epilepsy (such as phenytoin or carbamazepine).
- medicines for lowering blood pressure.
- barbiturates (for insomnia).
- thioridazine or lithium (antipsychotics).

- medicines that affect the heart rate, for instance, medicines that can cause an electrolyte imbalance (low levels of potassium and magnesium), such as diuretics or certain antibiotics (medicines for treatment of infections).
- medicines that can cause constipation.
- medicines (called “anticholinergics”), that affect the way nerve cells function in order to treat certain medical conditions.
- Anti-depressants. These medicines may interact with Seroquel XR and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, hallucinations, coma, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38°C (serotonin syndrome). Contact your doctor when experiencing these symptoms.

Before you stop taking any of your medicines, refer to the doctor.

Using this medicine and food

- Do not drink grapefruit juice during treatment with this medicine. Grapefruit juice can affect the way the medicine works.
- Seroquel XR can be affected by food. Therefore, take this medicine at least one hour before eating or prior to bedtime.

Using this medicine and alcohol consumption

Be careful how much alcohol you drink. This is because the combined effect of Seroquel XR and alcohol can make you sleepy.

Pregnancy and breastfeeding

If you are pregnant, think you may be pregnant, planning to become pregnant, or are breastfeeding, consult with a doctor before using this medicine. Do not take Seroquel XR during pregnancy unless you have discussed this with your doctor. Do not take Seroquel XR while you are breastfeeding.

The following withdrawal symptoms may occur in newborns of mothers who took Seroquel XR during the last trimester of pregnancy: tremor, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty eating. If your baby develops any of these signs, consult the attending doctor.

Driving and using machines

Using this medicine may make you feel sleepy. Do not drive or operate dangerous machines until you know how the medicine affects you.

Important information about some of this medicine’s ingredients

Seroquel XR contains lactose

The tablets contain lactose, which is a type of sugar. If you have been told by the doctor that you are unable to digest certain sugars, consult the doctor before taking this medicine.

Seroquel XR 50 mg - each tablet contains 125.72 mg lactose monohydrate.

Seroquel XR 150 mg - each tablet contains 74.65 mg lactose monohydrate.

Seroquel XR 200 mg - each tablet contains 52.87 mg lactose monohydrate.

Seroquel XR 300 mg - each tablet contains 49.31 mg lactose monohydrate.
Seroquel XR 400 mg - each tablet contains 15.50 mg lactose monohydrate.

Seroquel XR contains sodium

Seroquel XR 50 mg, Seroquel XR 150 mg, Seroquel XR 200 mg contain less than 23 mg sodium per tablet, that is to say essentially 'sodium-free'.

Seroquel XR 300 mg and Seroquel XR 400 mg contain 27 mg sodium (main component of table salt) in each tablet. This is equivalent to 1.35% of the recommended maximum daily intake of sodium for an adult.

Effect on Urine Drug Screens

- Seroquel XR can cause a positive result in urine tests for medicines that you are not taking, such as methadone or tricyclic antidepressants (TCAs). These results must be confirmed using further specific tests.

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 your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine. The doctor will adjust the daily dose of the medicine to range between 50 mg and 800 mg, depending on your disease and individual needs.

- **Do not exceed the recommended dose.**
- Take the tablets once a day.
- The dosage will be reduced gradually before stopping treatment.
- Do not stop treatment with the medicine even if you feel better, unless your doctor tells you.
- Take the medicine at least one hour before eating or before going to sleep.

Method of use:

- **Do not chew, do not crush, and do not halve the tablets!** Since the tablets are prolonged-release tablets.
- Swallow the tablets whole with water.
- Do not drink grapefruit juice while you are taking Seroquel XR. It can affect the way the medicine works.

Liver problems

If you have liver problems your doctor may change your dose.

Elderly

If you are elderly your doctor may change your dose.

Use in children and adolescents

This medicine is not intended for children and adolescents under the age of 18.

If you have accidentally taken a higher dose

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. You may feel sleepiness, dizziness, and abnormal heartbeat.

If you forget to take the medicine

If you forget to take the medicine at the scheduled time, take the dose as soon as you remember. Do not take a double dose under any circumstances. Adhere to the treatment as recommended by your doctor.

If you stop taking the medicine

Suddenly stopping the medicine may cause the following symptoms: insomnia, nausea, headache, diarrhea, vomiting, dizziness, and nervousness. Your doctor can recommend you to gradually reduce the dose before stopping treatment.

Do not take medicines in the dark! Check the label and the dose every time 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 Seroquel XR may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Very common side effects (appear in more than 1 in 10 users):

- Dizziness (may cause falls), headache, dry mouth.
- Sleepiness (may disappear with continued use of the medicine, may cause falls).
- Weight gain.
- Discontinuation Symptoms (symptoms which occur when you stop taking Seroquel XR) include: vomiting, dizziness, nausea, headache, diarrhea, insomnia and agitation. Gradual withdrawal over a period of 1 to 2 weeks is advisable.
- Abnormal muscle movements. These include difficulty starting muscle movements, shaking, restlessness, or muscle stiffness without pain.
- Changes in the levels of certain fats in the blood (triglycerides and cholesterol).

Common side effects (appear in 1-10 in 100 users):

- Rapid heart rate.
- Feeling that your heart is pounding, racing, or has skipped beats.
- Constipation, indigestion.
- Weakness.
- Swelling of the arms or legs.
- Low blood pressure in standing position which can result in being dizzy or feeling faint (may cause falls).
- Increase in blood sugar levels.
- Blurred vision.
- Unusual dreams, nightmares.
- Feeling more hungry.
- Nervousness.

- Disturbances in speech and language.
- Suicidal thoughts and exacerbated depression.
- Shortness of breath.
- Vomiting (mainly in the elderly).
- Fever.
- Changes in the levels of thyroid hormones in your blood.
- Decrease in the levels of certain types of blood cells.
- Increase in the level of liver enzymes measured in the blood.
- Increase in the level of the hormone prolactin in the blood. Increase in the hormone prolactin could in rare cases lead to the following:
 - Men and women to have swelling breasts and unexpectedly produce breast milk.
 - Women to have no monthly periods or irregular periods.

Uncommon side effects (appear in 1-10 in 1,000 users):

- Fits or seizures.
- Allergic reactions that may include raised lumps on the skin, swelling of the skin and swelling around the mouth.
- Restless-legs syndrome (unpleasant sensation in the legs).
- Difficulty swallowing.
- Uncontrollable movements, mainly of the face or tongue.
- Difficulties in sexual function.
- Diabetes.
- Change in the electric activity of the heart that is detectable in an ECG (prolongation of the QT interval).
- A slower than normal heart rate, which can occur upon starting treatment, and may be associated with low blood pressure and fainting.
- Exacerbation of existing diabetes.
- Difficulty urinating.
- Nasal congestion.
- Fainting (may cause falls).
- Decrease in the amount of red blood cells.
- Decrease in the amount of sodium in the blood.
- Confusion

Rare side effects (appear in 1-10 in 10,000 users):

- Combination of fever, sweating, muscle stiffness, acute tiredness or fainting (neuroleptic malignant syndrome).
- Yellowing of the skin and eyes (jaundice).
- Inflammation of the liver (hepatitis).
- Prolonged and painful erection.
- Swelling of breasts and unexpected production of breast milk.
- Blood clots in the veins, particularly in the legs (manifested by swelling, pain, and redness of the leg), which may travel in the blood stream to the lungs causing chest pain and difficulty in breathing. If you notice any of these symptoms seek medical advice immediately.

- Disruption of the menstrual cycle in women.
- Walking, talking, eating, and other activities, while asleep.
- Decrease in body temperature (hypothermia).
- Inflammation of the pancreas.
- Metabolic syndrome - a condition combining three or more of the following symptoms: increase in abdominal fat, decrease in 'good cholesterol' (HDL-C), increase in blood triglycerides, high blood pressure, and an increase in blood sugar level.
- Combination of fever, flu-like symptoms, sore throat, or any other infection together with a very low white blood cell count; a condition called agranulocytosis.
- Bowel obstruction.
- Increased blood creatine phosphokinase levels (a substance from the muscles).

Very rare side effects (appear in less than 1 in 10,000 users):

- Severe allergic reaction (called anaphylactic shock) that may include difficulty breathing and shock.
- Rapid swelling of the skin, usually around the eyes, lips, and throat (angioedema).
- Severe blistering of the skin, mouth, eyes, and genitals (Stevens-Johnson syndrome).
- Acute rash, blisters, or red patches on the skin.
- Abnormal secretion of the hormone that controls the volume of the urine.
- Breakdown of muscle fibers and muscle pain (rhabdomyolysis).

Side effects of unknown frequency:

- Rash with irregular red spots (erythema multiforme). See section 2.
Rapid appearance of areas of red skin studded with small pustules (small blisters filled with white/yellow fluid called Acute Generalized Exanthematous Pustulosis (AGEP). See section 2.
- Sudden acute allergic reaction with symptoms such as fever and blisters on the skin, and skin peeling (TEN - Toxic Epidermal Necrolysis). See section 2.
- DRESS syndrome - Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) which consists of flu-like symptoms with a rash, fever, swollen glands, and abnormal blood test results (including increased white blood cells (eosinophilia) and increased liver enzymes level). See section 2.
- Symptoms of withdrawal may occur in newborn babies of mothers that have used Seroquel XR during their pregnancy.
- Stroke.
- Disorder of the heart muscle (cardiomyopathy).
- Inflammation of the heart muscle (myocarditis).
- Inflammation of blood vessels (Vasculitis), often with skin rash with small red or purple bumps.

The class of medicines to which Seroquel XR belongs can cause disturbances in heart rate, which can be serious, and in severe cases may be fatal.

The following side effects have been observed in blood tests:

- Change in levels of fats in the blood (triglycerides and cholesterol).

- Change in blood sugar level.
- Changes in levels of thyroid hormones.
- Increase in the amount of liver enzymes.
- Decrease in the levels of certain types of blood cells.
- Decrease in the levels of red blood cells.
- Increase in creatine phosphokinase levels, a substance in the muscles.
- Decrease in blood sodium levels.
- Increase in the levels of the hormone prolactin in the blood. Rarely, this may lead to:
 - swelling of the breasts in men and women, and unexpected production of breastmilk.
 - in women, menstrual cycle stops or becomes irregular.

Your doctor may ask you to have blood tests from time to time.

If a side effect occurs, if any of the side effects worsen, or if you are suffering from a side effect not mentioned in this leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by following the “Reporting Side Effects of Drug Treatment” link found on the Ministry of Health home page (www.health.gov.il) which opens an online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il>

5. HOW TO STORE THE MEDICINE?

Prevent poisoning! To prevent poisoning, keep this medicine and all other medicines 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 your 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.

Do not store different medicines in the same package.

Do not store above 30°C.

6. ADDITIONAL INFORMATION

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

microcrystalline cellulose; lactose monohydrate; sodium citrate; hypromellose; magnesium stearate; titanium dioxide; polyethylene glycol 400; ferric oxide, yellow (50, 200 and 300 mg tablets); ferric oxide, red (50 mg tablets).

What the medicine looks like and contents of the pack:

Seroquel XR 50 mg tablets are capsule-shaped, bi-convex, peach-colored, with XR50 engraved on one side.

Seroquel XR 150 mg tablets are capsule-shaped, bi-convex, white in color, with XR150 engraved on one side.

Seroquel XR 200 mg tablets are capsule-shaped, bi-convex, yellow in color, with XR200 engraved on one side.

Seroquel XR 300 mg tablets are capsule-shaped, bi-convex, pale yellow in color, with XR300 engraved on one side.

Seroquel XR 400 mg tablets are capsule-shaped, bi-convex, white in color, with XR400 engraved on one side.

The package contains 10, 30, 50, 60 or 100 Tablets in a blister pack.

Not all pack sizes may be marketed.

Manufacturer's name and address:

CHEPLAPHARM Arzneimittel GmbH, Greifswald, Germany.

Registration holder's name and address:

Tzamal Bio-Pharma Ltd., 20 Hamagshimim St., Petah Tikva.

Registration number of the medicine in the Ministry of Health's National Drug Registry:

Seroquel XR 50 mg: 1418931973

Seroquel XR 150 mg: 1469733472

Seroquel XR 200 mg: 1419031974

Seroquel XR 300 mg: 1419131975

Seroquel XR 400 mg: 1419231976

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