

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

The medicine is dispensed with a doctor's prescription only

**SEROQUEL® 25 mg
Film-coated tablets**

**SEROQUEL® 100 mg
Film-coated tablets**

**SEROQUEL® 200 mg
Film-coated tablets**

**SEROQUEL® 300 mg
Film-coated tablets**

The active ingredient and its quantity:

Each tablet of Seroquel 25 mg contains:
quetiapine (as fumarate) 25 mg

Each tablet of Seroquel 100 mg contains:
quetiapine (as fumarate) 100 mg

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

Each tablet of Seroquel 300 mg contains:
quetiapine (as fumarate) 300 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 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 illness is similar to yours. This medicine is not intended for children and adolescents below 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 in children, adolescents and young adults up to the age of 25. Upon initiation of treatment with the medicine, patients of all ages, and their relatives, must monitor behavioral changes such as worsening of depression, suicidal thoughts, aggressiveness and the like. If such changes occur, refer to a doctor immediately.
- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.

1. WHAT IS THIS MEDICINE INTENDED FOR?

- Treatment of schizophrenia.
- Treatment of manic episodes associated with bipolar disorder.
- Treatment of major depressive episodes in bipolar disorder.

Seroquel is not indicated for the prevention of recurrence of manic or depressive episodes.

Therapeutic group – antipsychotic medicines.

Schizophrenia is an illness where you may hear or feel things that do not exist, believe things that are not true or feel unusually suspicious, anxious, confused, guilty, tense or depressed. Mania is a condition in which you may feel very excited, elated, agitated, enthusiastic, hyperactive or experience a decline in your sense of judgment and aggressiveness. Bipolar disorder is a condition in which you may feel sad all the time or you find that you are depressed, have feelings of guilt, lack energy, lose your appetite or are unable to sleep. The doctor may continue your treatment with Seroquel even if you are feeling better.

2. BEFORE USING THE 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 'Additional information').
 - you are taking the following medicines:
 - Medicines for treatment of 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.

Special warnings about using Seroquel

Before treatment with Seroquel, tell your doctor if:

- you or a family member have or have had heart problems such as heart rhythm problems, weakening of the heart muscle or inflammation of the heart 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 in a risk group of getting diabetes. If you do, your doctor may check your blood sugar levels while you are taking Seroquel.
- you had in the past a low white blood cell levels (which may have been caused by other medicines).
- Do not take Seroquel if you are an elderly person with dementia, because Seroquel may increase the risk of stroke, or in some cases it may increase the risk of death in elderly people with dementia.
- you are an elderly person with Parkinson's disease/parkinsonism.
- you or someone else in your family has a history of blood clots, as medicines like Seroquel have been associated with formation of blood clots.
- you have or have had a condition where you stop breathing for short periods during your normal 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 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:

- a combination of fever, acute muscle stiffness, sweating, or reduced consciousness (this is a disorder called “neuroleptic malignant syndrome”). You may need urgent medical treatment.
- involuntary movements, mainly of the face and tongue.
- dizziness or a severe sense of feeling sleepy, which can increase the risk of accidental injury (falls) in elderly people.
- seizures.
- long lasting and painful erection.
- 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.

The above-mentioned conditions can be caused by using the type of medicines Seroquel belongs to.

Inform the doctor as soon as possible if you feel any of the following:

- 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 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 condition of blockage of the bowel.
- Suicidal thoughts and exacerbated depression: If you are depressed you may sometimes have suicidal thoughts. These may be increased when first starting treatment with Seroquel, since it takes time for the medicine to work, usually about two weeks but sometimes longer. Increased suicidal thoughts may also be increased if treatment with Seroquel is suddenly stopped. These thoughts are more common among 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 with depression. If you have thoughts of harming or killing yourself 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 which can be life threatening or fatal have been reported rarely in patients who take Seroquel. These are commonly manifested by the following symptoms:
 - Stevens-Johnson Syndrome (SJS), a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals.

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

Stop using Seroquel 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. You and your doctor should check your weight regularly.

Children and adolescents

This medicine is not for use in children and adolescents below 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 if you are taking any of the following medicines:

- Medicines for treatment of acquired immune deficiency syndrome (AIDS).
- Medicines from the azole family (for treatment of fungal infections).
- Erythromycin or clarithromycin (for treatment of infections).
- Nefazodone (for treatment of depression).

Inform the doctor if you are taking:

- Epilepsy medicines (like phenytoin or carbamazepine).
- High blood pressure medicines.
- Barbiturates (for difficulty sleeping).
- Thioridazine or lithium (anti-psychotic medicines).
- Medicines that have an impact on the way your heart beats, for example, drugs that can cause an imbalance in electrolytes (low levels of potassium and magnesium) such as diuretics or certain antibiotics (drugs to treat 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 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, please talk to your doctor first.

Using this medicine and food

Seroquel can be taken with or without food. Do not drink grapefruit juice during treatment with Seroquel. Grapefruit juice may affect the way the medicine works.

Using this medicine and alcohol consumption

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

Pregnancy and breastfeeding

Before taking Seroquel, inform the doctor if you are pregnant, planning to become pregnant, or are trying to become pregnant. Do not take Seroquel during pregnancy unless you have discussed this with your doctor. Do not take Seroquel if you are breastfeeding. The following withdrawal symptoms may occur in newborns of mothers who took Seroquel 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 symptoms you must consult the doctor.

Driving and using machines

Use of this medicine may cause sleepiness. Do not drive or use machines until you know how the medicine affects you.

Important information about some of this medicine's ingredients

Seroquel tablets contain lactose. Lactose is a type of sugar. If you have lactose intolerance or you are unable to digest certain sugars, please inform your doctor before taking Seroquel.

Seroquel 25 mg - each tablet contains 19.00 mg lactose monohydrate.

Seroquel 100 mg - each tablet contains 20.70 mg lactose monohydrate.

Seroquel 200 mg - each tablet contains 41.40 mg lactose monohydrate.

Seroquel 300 mg - each tablet contains 62.10 mg lactose monohydrate.

Seroquel tablets contain less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Effect on urine drug screens: Seroquel may cause a positive result in a urine drug screen for medicines you are not taking, such as methadone or certain drugs for depression called tricyclic antidepressants (TCAs). Those results should be confirmed with additional tests.

3. HOW TO USE THIS MEDICINE?

- Always use according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure. Only your doctor or pharmacist will determine your dose and how you should take this medicine.
- The doctor can adjust the daily dose of the medicine between 150 mg to 800 mg, according to your individual illness and needs.
- **Do not exceed the recommended dose.**
- You will take your tablets once a day, at bedtime or twice a day, depending on your illness.

Method of use

- Swallow the tablets whole with water regardless of food.
- There is no data regarding crushing/halving/chewing.

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

Elderly people: If you are elderly your doctor may change your dose.

If you have accidentally taken a higher dose: If you have accidentally 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 tiredness, dizziness, and abnormal palpitations.

If you forget to take the medicine: If you forget to take this medicine at the scheduled time, do not take a double dose. Take a dose as soon as you remember. Take the next dose at the regular time and consult the doctor. Adhere to treatment as recommended by your doctor.

If you stop taking this medicine: Do not stop treatment with the medicine even if you feel better, unless the doctor instructs you to. Suddenly stopping the medicine may cause the following symptoms: insomnia, nausea, headache, diarrhea, vomiting, dizziness and irritability. Your doctor may suggest you reduce the dose gradually 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 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 lead to falls), headache, dry mouth, feeling sleepy (may lead to falls) (this may go away with time, as you keep taking the medicine), discontinuation symptoms - insomnia, nausea, headache, diarrhea, vomiting, dizziness and irritability. Gradual withdrawal over a period of at least 1 to 2 weeks is advisable. Weight gain, abnormal muscle movements, including difficulty starting muscle movements, tremor, feeling restless 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):

Fast heartbeat, feeling like your heart is pounding, racing or has skipped beats, indigestion or constipation, weakness, swelling of arms or legs, high levels of sugar in the blood, low blood pressure when standing up (may make you feel dizzy or faint and lead to falls), blurred vision, abnormal dreams and nightmares, feeling hungrier, feeling irritated, speech disturbance, thoughts of suicide and worsening of depression, shortness of breath, vomiting (mainly in the elderly), fever, changes in the amount of thyroid hormones in the 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 sensations in the legs), difficulty swallowing, uncontrollable movements, mainly of the face and tongue, sexual dysfunction, diabetes, change in electrical activity of the heart seen on ECG (QT prolongation), a slower than normal heart rate which may occur when starting treatment and which may be associated with low blood pressure and fainting, difficulty in passing urine, fainting (may lead to falls), stuffy nose, decrease in the amount of red blood cells, decrease in the amount of sodium in the blood, worsening of pre-existing diabetes, confusion.

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

A combination of fever, sweating, stiff muscles, feeling very drowsy or faint (neuroleptic malignant syndrome), yellowing of the skin and eyes (jaundice), inflammation of the liver (hepatitis), a long-lasting and painful erection, swelling of breasts and unexpected production of breast milk, menstrual disorder, blood clots in the veins, especially in the legs (symptoms include leg swelling, pain and redness), which may travel through blood vessels to the lungs causing chest pain and difficulty breathing. If you notice any of these symptoms seek medical assistance immediately, walking, talking, eating or other activities while you are asleep, body temperature decreased (hypothermia), inflammation of the pancreas, metabolic syndrome - a condition in which you may have a combination of 3 or more of the following symptoms: an increase in fat around the abdomen, a decrease in "good cholesterol" (HDL-C), an increase in blood triglycerides, high blood pressure and an increase in blood sugar levels, combination of fever, flu-like symptoms, sore throat or any other infection with 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 one in 10,000 users):

Severe rash, blisters and red patches on the skin, a severe allergic reaction which may cause difficulty in breathing or anaphylactic shock, rapid swelling of the skin, usually around the eyes, lips and throat (angioedema), a serious blistering condition of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome) see the Warning section, abnormal secretion of a hormone that controls urine volume, breakdown of muscle fibers and pain in muscles (rhabdomyolysis).

Side effects with unknown frequency:

Skin 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. Serious, sudden allergic reaction with symptoms such as fever, blisters on the skin and peeling of the skin (TEN), see section 2, DRESS - drug reaction with eosinophilia and systemic symptoms, which consists of flu-like symptoms with a rash, fever, swollen glands, and abnormal blood test results (including increased white blood cells (eosinophilia) and liver enzymes), see section 2, symptoms of withdrawal may occur in newborn babies of mothers who used Seroquel 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 belongs can cause heart rhythm problems, which can be serious and in severe cases may be fatal.

The following side effects have been observed in blood tests:

Changes in the levels of certain fats (triglycerides and total cholesterol), increase in blood sugar levels, changes in the amount of thyroid hormones in your blood, increased liver enzymes, decrease in the levels of different types of blood cells, decrease in the levels of red blood cells, decrease in the levels of sodium in the blood, increased blood creatine phosphokinase (a substance in the muscles). 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 of the breasts and unexpectedly produce breast milk. Women to have no monthly period or irregular periods.

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

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned here, please consult your doctor immediately.

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or you can also use this 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 above 30°C.

6. ADDITIONAL INFORMATION

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

microcrystalline cellulose, lactose monohydrate, calcium hydrogen phosphate dihydrate, sodium starch glycollate type A, povidone, magnesium stearate, methylhydroxypropyl cellulose, titanium dioxide (E171), macrogol 400, ferric oxide, yellow (E172) (present only in the 25 mg and 100 mg tablets), ferric oxide, red (E172) (present only in the 25 mg tablets).

What the medicine looks like and contents of the pack:

Seroquel 25 mg film-coated tablets are round, bi-convex, peach-colored, with 'Seroquel 25' engraved on one side, and the other side blank.

Seroquel 100 mg film-coated tablets are round, bi-convex, yellow in color, with 'Seroquel 100' engraved on one side, and the other side blank.

Seroquel 200 mg film-coated tablets are round, bi-convex, white in color, with 'Seroquel 200' engraved on one side and the other side blank.

Seroquel 300 mg film coated tablets are capsule-shaped, bi-convex, white in color, with '300' engraved on one side and 'Seroquel' on the other.

Seroquel 25 mg packages contain 8, 20, 30, 50, 60 or 100 film-coated tablets in a blister pack.

Seroquel 100 mg packages contain 8, 10, 30, 50, 60, 90 or 100 film-coated tablets in a blister pack.

Seroquel 200 mg packages contain 30, 50, 60, 90 or 100 film-coated tablets in a blister pack.

Seroquel 300 mg packages contain 10 or 30 film-coated tablets in a blister pack.

Not all pack sizes may be marketed.

Registration holder's name and address: Tzamal Bio-Pharma Ltd., 20 Hamagshimim St., Petah Tikva.

Manufacturer's name and address: CHEPLAPHARM Arzneimittel GmbH, Greifswald, Germany.

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

Seroquel 25 mg: 109 39 29313 00

Seroquel 100 mg: 109 40 29314 00

Seroquel 200 mg: 109 41 29315 00

Seroquel 300 mg: 135 33 31257 00

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