

# CLOZARIL<sup>®</sup>

Clozapine 25 mg or 100 mg tablets

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## What Clozaril is used for

Clozaril tablets contain an active substance called clozapine. This medicine belongs to a group of medicines called antipsychotics. Clozaril is used to treat people suffering from schizophrenia who have either tried other antipsychotic medications and did not benefit sufficiently or who are unable to tolerate other antipsychotic medications because of side effects.

Clozaril is also used to treat people suffering from schizophrenia or schizoaffective disorder (schizophrenia with mood disorders) who might otherwise attempt to commit suicide. Schizophrenia is a mental illness involving disturbances in thinking, emotional reactions, and behavior.

In addition, Clozaril is used to treat thought, emotional and behavioral disturbances in patients with Parkinson's disease, when standard treatment has failed. Parkinson's disease is a chronic (persistent) disorder of the brain. It mainly affects the way the brain co-ordinates the movements of the muscles in various parts of the body.

## How Clozaril works

Clozaril predominantly works by binding to and blocking the D4 receptor (or dopamine receptor) in the brain. Clozaril also has weak binding and blocking activity on the D1, D2, D3 and D5 receptors in the brain as well as other

receptors that potentially have some contribution to its effectiveness.

## Before you use Clozaril

Clozaril may only be taken if prescribed by a doctor. Follow all doctor's instructions carefully, even if they differ from the general information contained in this leaflet. Before starting Clozaril, you will have a blood test to make sure that you can take this medicine.

## When you must not use it

- If you are allergic to clozapine or any of the ingredients of Clozaril listed at the beginning of this leaflet.
- If you are unable to undergo regular blood tests.
- If you have ever been diagnosed with low white blood cells except if it was following a treatment for cancer.
- If you suffer or have ever suffered from bone marrow disease.
- If you have liver, kidney or heart problems.
- If you suffer from uncontrolled seizures.
- If you have problems with alcohol or drug abuse.
- If you suffer or have ever suffered from severe constipation, obstruction of the bowel or any other condition which has affected your large bowel.

If any of the above applies to you, tell your doctor without taking Clozaril.

If you think you are allergic to Clozaril (clozapine), ask your doctor for advice before taking Clozaril.

## Pregnancy and lactation

Tell your doctor or pharmacist before using Clozaril if you are pregnant, or you think that you may be pregnant. Your doctor will discuss with you the benefits and potential risks of using this medicine during pregnancy. Tell your doctor immediately if

you become pregnant during Clozaril treatment. Newborn babies of mothers taking antipsychotic drugs during the third trimester of pregnancy may have increased risk of developing stiff limbs, trembling, agitation, muscle stiffness, muscle flaccidity, drowsiness, short and shallow breathing, and feeding disorders following delivery. In some cases, these symptoms may be self-limiting, in other cases, babies may require intensive care unit support or hospitalization.

Tell your doctor or pharmacist if you are breast-feeding. *Clozapine*, the active ingredient of Clozaril, may pass into your milk and affect your baby. You should not breast-feed during Clozaril treatment.

## Before you start to use it:

Talk to your doctor or pharmacist if you:

- Have or at a risk of having diabetes (e.g., being overweight or a family history of diabetes). Your doctor should check your blood sugar before you start using Clozaril and regularly during treatment.
- If you have had a stroke, heart disease or family history of abnormal conduction in the heart called "prolongation of the QT interval"
- If you suffer from enlargement of the prostate, convulsions, glaucoma (a condition in which the pressure of fluid in the eye is generally too high) or any other serious medical condition.

If any of these apply to you, tell your doctor before you take Clozaril.

Taking Clozaril with food and drink

- Interaction with alcohol: Clozaril may enhance the effects of alcohol. You should not drink

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alcohol while taking Clozaril.

- Levels of Clozaril in the blood can be affected by stopping smoking or changing in the number of caffeine-containing drinks you have in a day. Inform your doctor of any such changes in your habits.

Older people (age 60 years and over). Your doctor might need to adjust your treatment if you are 60 or older.

Tell your doctor or pharmacist if you suffer from a condition called dementia.

**Children and adolescents**, the use of Clozaril in children and adolescents is not recommended.

**Women of child-bearing potential and contraception** Some women taking some antipsychotic medications have irregular or no periods. If you are female and you have been affected in this way, your periods may return when your medication is changed to Clozaril. In these circumstances, you should make sure that you use a reliable method of contraception.

## Taking other medicines

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. Remember those not prescribed by a doctor. This includes sleeping pills, tranquilizers, anti-allergy medicines, antibiotics, medicines used to treat depression, convulsions or ulcers of the stomach, and medicines effective against fungal or viral infections, other medicines used to treat mental illness, birth-control tablets. These medicines can interfere with your treatment.

Tell your doctor or pharmacist if you are taking or have recently taken

medicines which cause constipation (such as anticholinergic, which are used to relieve stomach cramps, spasms, and travel sickness)

## **How to use Clozaril**

Follow your doctor's instructions carefully. Do not exceed the recommended dosage.

Take Clozaril tablets by mouth. The scored tablets can be divided into equal halves (the formulation may differ in some countries).

## How much to use

Your doctor will tell you exactly how many tablets of Clozaril to take and how often you should take them.

- Treatment of schizophrenia or schizoaffective disorders in people who might otherwise attempt to commit suicide  
Treatment is usually started with one half of a 25 mg tablet (12.5 mg) once or twice on the first day. Your doctor will then gradually increase your dose, until the ideal dose for you is established.  
Your treatment will continue with a daily dose of Clozaril between 300 and 450 mg. The daily dose is usually taken in divided portions, some being taken in the morning and some at bedtime. Some people may require doses of up to a maximum of 900 mg per day.
- Treatment of thought, emotional and behavioral disturbances in patients with Parkinson's disease  
Treatment is usually started with one half of a 25 mg tablet (12.5 mg) in the evening, and then the dose will be gradually increased until the ideal dose for you is established.
- Your treatment will continue with a daily dose of Clozaril between 25 mg and 37.5 mg and will usually be given as a

single dose each evening. Some people may require doses of up to 50 mg per day. In exceptional cases, your doctor may prescribe a higher dose but the dose must never exceed 100 mg per day.  
Your blood pressure will be measured during the first weeks of treatment.

## When to use Clozaril

Taking Clozaril at the same time each day will help you remember when to take your medicine.

## How long to use Clozaril

Continue taking Clozaril as your doctor tells you.

If you have questions about how long to take Clozaril, talk to your doctor or your pharmacist.

## If you forget to use Clozaril

If you forget to take a dose, take another as soon as you remember. However, if it is time to take your next dose, or less than 4 hours before your next dose, leave out your forgotten tablets and take your next dose at the right time. Do not take a double dose of Clozaril to make up for the one that you missed.

If you have not taken Clozaril for more than two days, do not re-start taking the medicine and contact your doctor as soon as possible.

## If you use more Clozaril than you should (overdose)

If you have accidentally taken too many tablets, talk to your doctor or pharmacist straight away. You may require medical attention.

## **While you are using Clozaril**

### Things you must do

#### *Monitoring during your treatment with Clozaril*

You will have regular blood tests for as long as you continue to take Clozaril and for four weeks after stopping the treatment. Your doctor will tell you when to have the tests. It is important that you attend for all blood tests recommended by your doctor.

If you suffer from high level of sugar in the blood (diabetes) your

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doctor may regularly check your level of sugar in the blood. Clozaril may cause alteration in blood lipids. Clozaril may cause weight gain.

Your doctor may monitor your weight and blood lipid levels. If you have any questions about how Clozaril works or why this medicine has been prescribed for you, ask your doctor.

- Consult your doctor immediately at the first sign of a cold, influenza, fever, sore throat, or any other infection. Clozaril can reduce the number of white cells in your blood, and lead to a higher sensitivity to infection. Your doctor may check your blood cell count and take further measures if necessary.
- Consult your doctor immediately if you experience fast and irregular heartbeat that persists when you are at rest, possibly accompanied by shortness of breath and swelling of the feet or legs. These effects may especially occur at the beginning of the treatment and your doctor may need to take further measures.

During treatment with Clozaril you may experience:

- Light-headedness or fainting, especially at the start of treatment. This is due to a lowering of your blood pressure.
- Seizures, drowsiness, fainting, muscle weakness, which may lead to falls
- Chest pain which may be a symptom of heart attack which may lead to death.
- Chest pain which may be due to inflammation of the heart muscle which may

lead to death

- Abdominal pain and constipation which may be a sign of abnormal dilatation of the large intestines which may lead to death
- Abdominal pain which could be a sign of breakdown of part of the intestine due to its compromised blood supply which may lead to death.
- Sleepiness and remaining in bed for prolonged duration in combination with weight gain which may lead to blood clots in some patients

If you get any of these symptoms, tell your doctor straight away.

Tell your doctor or pharmacist if you have experienced constipation, abdominal pain, abdominal tenderness, fever, bloating and/or bloody diarrhea. Your doctor will need to examine you

## **Things you must not do** **If you stop taking Clozaril** **Risk for withdrawal effects**

Do not suddenly stop using Clozaril.

If this medicine must be stopped for any reason, your doctor will reduce the dose gradually over a 1- to 2-week period to avoid side effects. Suddenly stopping Clozaril or rapidly reducing the dose can cause side effects.

For this reason, it is very important that you, and those caring for you, are able to recognize signs of Clozaril withdrawal.

If sudden discontinuation of Clozaril is necessary, the patient may have psychotic symptoms and withdrawal symptoms such as profuse sweating, headache, nausea, vomiting and diarrhea. If you have any of the above signs, tell your doctor straight away. These signs may be followed by more serious side effects unless you are treated

immediately.

## **Things to be careful of** **Driving and using machines**

Clozaril may cause drowsiness, especially at the start of treatment. Therefore, you should avoid driving or using machines until you have got used to the medication and drowsiness has disappeared.

## **Side effects**

**Talk to your doctor or pharmacist if you experience:**

- Increase in blood sugar level and/or symptoms of high blood sugar (e.g., increased thirst, increased hunger, and frequent urination)
- Unpleasant leg sensations and an intense urge to move the legs (*restless legs syndrome*)
- Trouble breathing during sleep (*sleep apnoea*)
- Difficulty or inability to pass urine (*urinary retention*)

Tell your doctor or pharmacist as soon as possible if you get any unexpected symptoms while you are using Clozaril, even if you do not think that they are connected with the medicine.

Some side effects could be serious and need medical attention

*Very common: these side effects may affect more than 10 in every 100 patients*

Fast heartbeat

*Common: these side effects may affect between 1 and 10 in every 100 patients*

- Signs of infection such as fever, severe chills, sore throat or mouth ulcers. Clozaril can reduce the number of white cells in your blood, and lead to a higher sensitivity to infection.
  - Seizures.
  - High level of a specific type of white blood cells, increased white blood cell count.
  - Loss of consciousness, fainting.
- Uncommon: these side effects may affect between 1 and 10 in every 1,000 patients*
- Fever, muscle cramps, fluctuation in blood

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pressure, disorientation, confusion.

If you experience any of these, tell your doctor immediately.

**Some side effects are very common.** These side effects may affect more than 10 in every 100 patients

- Drowsiness
- Dizziness
- Constipation and failure to pass gas (bowel obstruction), tell your doctor if constipation gets worse.
- Abdominal pain, swollen abdomen
- Increased production of saliva

**Some side effects are common.** These side effects may affect between 1 and 10 in every 100 patients

- Weight gain
- Slurred speech
- Abnormal movements, inability to initiate movement, inability to remain motionless, inner feeling restlessness, stiff limbs, trembling hands.
- Shaking/trembling
- Muscle stiffness
- Headache
- Blurred vision, difficulties in reading
- Changes in ECG heart machine
- Lightheadedness upon standing due to decreased blood pressure
- Increase in blood pressure
- Nausea, vomiting, dry mouth
- Elevated liver enzymes
- Problems in passing or retaining urine
- Fever
- Tiredness

Contact your doctor if any of these affect you severely. If you notice any side effects not mentioned in this leaflet, inform your doctor or pharmacist.

You may report any side

effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website [npra.gov.my](http://npra.gov.my) [Consumers -> Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)]”.

## Storage and disposal of Clozaril

### - Storage

- Keep Clozaril out of the reach and sight of children.
- Store in the original package.
- Do not use Clozaril after the expiry date shown on the pack.
- Do not use any Clozaril pack that is damaged or shows signs of tampering.
- Store below 30°C

### - Disposal

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## Product Description

### What it looks like

Clozaril tablet 25mg: Yellow, circular, flat-beveled edge tablet with facilitated parting line and coded LO on one side, marked SANDOZ (circle) on the other. Clozaril tablet 100mg: Yellow, circular, flat-beveled edge tablet with facilitated parting line and coded ZA on one side, marked SANDOZ (linear) on the other.

Each tablet contains 25 mg or 100 mg clozapine. The scored tablets can be divided into equal halves (the formulation may differ between countries or regionally).

This information might differ in some countries.

## Ingredients

### - Active ingredients

The active substance of lozaril is clozapine.

### - Inactive ingredients

The other ingredients are magnesium stearate, silica, colloidal anhydrous, povidone, talc, maize starch, and lactose monohydrate.

## MAL Number:

Clozaril Tablet 25mg:  
MAL19992681ARZ

Clozaril Tablet 100mg:  
MAL20000747ARZ

## Manufacturer:

MADAUS GmbH  
Lutticher Strasse 5,53842 Troisdorf,  
Germany.

## Product Registration Holder:

Mylan Healthcare Sdn Bhd  
15-03 & 15-04, Level 15, Imazium,  
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Selangor.

## Date of revision: May 2023

Serial number:  
NPRA (R1/6)13072023/132