

Clozapine (Clozaril®)



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Summary: Clozapine (Clozaril®, Apo-clozapine®, Gen-clozapine®) belongs to a group of medications called “atypical antipsychotics” or “second-generation antipsychotics”.

What is clozapine used for?

Clozapine is used to reduce the symptoms of schizophrenia or psychosis (thought disorders) in those who have not responded well to other antipsychotic medications. Clozapine has specifically been shown to be helpful when other antipsychotics have not worked. In adults, clozapine has been found to reduce symptoms of schizophrenia to a greater extent than other antipsychotics.

Clozapine may also be helpful in treating other psychiatric conditions such as:

- Bipolar disorder
- Schizoaffective disorder
- Impulsive/aggressive behaviors (associated with psychotic disorders)
- Obsessive compulsive disorder (OCD)

Your doctor may be using this medication for another reason. If you are unclear why this medication is being prescribed, please ask your doctor.

How does clozapine work?

Like other atypical antipsychotics, clozapine affects the levels of certain chemicals in the brain called dopamine and serotonin. This has been shown to help people who have disorders like schizophrenia and bipolar disorder with their symptoms. The exact way that antipsychotics improve the symptoms of schizophrenia and bipolar disorder is not fully known.

Clozapine in Children and Adolescents

Clozapine is mainly used in adults, but under certain circumstances, it may be prescribed for children and adolescents.

Like many medications used to treat childhood disorders, clozapine has not been formally approved by Health Canada for use in children and adolescents. Testing of clozapine in research studies in children and adolescents has been limited. However, current evidence shows benefit for clozapine when used in children and adolescents who have previously failed to respond to other medications (usually 2 or more)

for the treatment disorders such as schizophrenia or bipolar disorder. In a 6-week trial of clozapine in children and adolescents with schizophrenia who did not get better with previous treatment, 40% of the patients improved. Clozapine appears to be particularly helpful in decreasing the aggressive behaviors and psychotic symptoms of these disorders.

How should clozapine be taken?

Clozapine is usually taken once or twice a day with or without food. This medication should be taken at the same time each day as directed by your doctor. Try to connect it with something you do each day (like eating breakfast or brushing your teeth) so that you don't forget. Try to avoid alcohol and limit drinks with caffeine (i.e. coffee, tea, energy drinks, colas) while taking clozapine. Do not take any antacids (such as Maalox® or Tums®) within 2 hours of your clozapine dose. You can take this medication with milk, water, orange or apple juice. However, avoid taking clozapine with grapefruit or related citrus juice or fruit (as these may interact with clozapine) or high calorie soft drinks.

Usually, your doctor will start with a low dose of clozapine that is best suited to your age and weight. This dose will then be slowly increased over several days or weeks based on how you respond to it. You and your doctor can then discuss the best dosage to stay on based on how you tolerate this medication (how well it helps decrease your symptoms and how you are doing with side effects).

When will clozapine start working?

When treating the symptoms of schizophrenia (such as hallucinations or delusions), it usually takes 3 to 6 weeks or longer before the benefits of clozapine are noticeable. The full effects of clozapine may not be seen until after 6 to 12 months. When clozapine is working well, you may notice that your thoughts are clearer and more organized. Agitation may be decreased and hearing voices or seeing things no one else sees (hallucinations) may stop completely or happen much less. Your mood may be more settled and you may see a reduction of intense fears and worries. Some people may even begin to feel less agitated within the first week of starting this medication.

Medications like clozapine do not work for everyone. If a noticeable improvement is not seen within a couple months, or if the side effects are too troublesome, your doctor may discuss other treatment options with you (i.e. switching you to a different medication).

How long do I have to take clozapine?

This depends on the symptoms you have, how frequently they occur, and how long you have had them. If you have had symptoms of schizophrenia (on and off) for several years, and you are not having too many side effects, your doctor may recommend you take clozapine indefinitely.

As it takes several months to see the full benefits of taking clozapine, you should NOT decrease, increase the dose or stop taking this medication (even if you feel better) without discussing it with your doctor. It is possible that your symptoms may return or you may have a bad reaction.

Is clozapine addictive?

No, clozapine is not addictive and you will not have "cravings" for this medication like you might with nicotine or street drugs. If you and your doctor decide it is best for you to stop taking clozapine, your doctor will explain how to safely come off this medication so you don't feel negative effects as your body adjusts to being without it.

Why do I have to have regular blood tests while I am taking clozapine?

Clozapine is known to cause a rare but serious side effect called "agranulocytosis". This side effect occurs in less than 1 out of every 100 people who take clozapine. This side effect can result in a decrease in the number of infection-fighting cells (called white blood cells or neutrophils) in your body. Without enough infection-fighting cells, your body may not be able to properly fight off infections, and you could become very sick. To start, your doctor will

order a blood test once weekly to check your white blood cell and neutrophil count.

If your white blood cell and/or neutrophil count is dropping, you may be asked to temporarily have blood testing done twice a week. If your blood counts continue to drop, or become very low, you may need to stop taking clozapine. If this happens, your doctor will explain how to safely come off this medication. If this happens, stopping clozapine allows your body to make more infection-fighting cells so you are able to fight off infection.

After taking clozapine for 6 months, the risk of this side effect on white blood cells and neutrophils decreases. At this point, blood tests are required every 2 weeks (instead of every week). If you have taken clozapine for one year or more and your white blood cell and neutrophil count are stable, blood testing may be done once per month.

What are the side effects of clozapine and what should I do if I get them?

As with most medications, side effects may occur when taking clozapine. Sometimes the side effects may occur before any of the beneficial effects. It is also possible for some individuals to experience side effects that they feel are serious or long lasting. If this occurs, speak to your doctor about ways to manage them. Here are some of the more common side effects of taking this medication. In brackets are suggested ways to lessen these effects.

Common side effects

Side effects are usually more common when starting a medication or after a dose increase. If any of these side effects is troublesome for you, please discuss them with your doctor, nurse or pharmacist.

- Blurred vision (usually disappears 1-2 weeks after last dose increase; use bright light or a magnifying glass to read)
- Constipation (increase exercise, fluids, vegetables, fruits and fiber; if severe, talk with your doctor about medications)
- Dizziness (may be worse after starting or a dose increase; try getting up slowly from a sitting or lying down position)
- Drowsiness (try taking the dose at bedtime)
- Dry mouth (try chewing sugarless gum, sour candies, ice chips, or popsicles)
- Excessive drooling (often occurs at night; other medications may help this; talk to your doctor)
- Headache (try using a pain reliever like acetaminophen (plain Tylenol®))
- Increase in hunger (avoid high calorie foods)
- Stomach ache (try taking the medication with food)
- Weight gain (monitor your food intake, increase your exercise)

Uncommon side effects (e.g., those that occur in less than 5% of patients)

Contact your doctor IMMEDIATELY if you have any of these side effects:

- Chest pain
- Confusion
- Difficulty urinating
- Fainting
- Fast or irregular heart beat
- Fever
- Flu-like symptoms (do not delay; this may be related to low white blood cell count)
- Frequent urination accompanied by excessive thirst
- Mouth soreness
- Rash or swelling
- Seizures
- Shortness of breath or difficulty breathing
- Sore throat or other signs of infection (do not delay; this may be related to low white blood cell count)
- Stiff muscles

- Uncontrollable or unusual movements

Your doctor will also have you do regular blood tests to check for other side effects, such as effects on lipids (e.g. cholesterol, triglycerides) and glucose (blood sugar).

Clozapine is sometimes associated with a very rare side effect called “neuroleptic malignant syndrome”. The symptoms may include severe muscle stiffness, high fever, increased heart rate and blood pressure, irregular heartbeat (pulse) and sweating. Contact your doctor right away if this occurs.

What precautions should my doctor and I be aware of when taking clozapine?

Tell your doctor or pharmacist if you:

- Have any allergies or have experienced a reaction to a medication.
- Are taking or plan to start taking any other prescription or non-prescription medications (including herbal products). Some medications can interact with clozapine, such as some sedatives, blood pressure medications, some antibiotics and several others. Your doctor may need to change the doses of your medications or monitor you carefully for side effects if you are taking medications that interact with clozapine.
- Have a history of heart disease, have epilepsy or have ever had a seizure, kidney or liver disease, bowel obstruction, glaucoma or diabetes (or a family history of diabetes).
- Miss a period, are pregnant (or are planning to become pregnant) or are breast-feeding.
- Currently smoke cigarettes or have recently stopped smoking cigarettes, use alcohol or street drugs as these substances can decrease how well clozapine works for you and/or make you feel more drowsy.

What special instructions should I follow while using clozapine?

- Keep all appointments with your doctor and the laboratory. Your doctor may order certain lab tests (such as glucose or prolactin levels, lipid levels, or liver tests) to check how you are responding to clozapine.
- Do not allow anyone else to use your medication.
- Try to keep a healthy and well balanced diet along with regular exercise. Some individuals who take clozapine may gain weight due to an increase in appetite.
- If you experience abnormal movements in your arms, legs, body or face, tell your doctor as soon as possible.

What should I do if I forget to take a dose of clozapine?

If you take clozapine only at bedtime and you forget to take it, skip the missed dose and continue with your regular schedule the next day. Do NOT double your next dose. If you take it more than once a day, take the missed dose as soon as possible. However, if it is almost time for your next dose (e.g., within 4 hours), skip the missed dose and continue with your regular schedule. Do NOT double your next dose.

What storage conditions are needed for clozapine?

- Keep this medication in the original container, stored at room temperature away from moisture and heat (e.g., not in the bathroom or kitchen).
- Keep this medication out of reach and sight of children.

Share this information

You may wish to share this information with your family members to help them to understand your treatment options. Since every person's needs are different, it is important that you follow the advice provided to you by your own doctor, nurse and/or pharmacist and speak to them if you have any questions about this medication.

About this document

Special thanks to the Kelty Centre for Mental Health for permission to adapt this document. The original document was developed by health professionals of BC Mental Health and Addiction Services, and reviewed by the staff of the Kelty Mental Health Centre. French translation provided courtesy of the Ontario Centre of Excellence for Child and Youth Mental Health and the Children's Hospital of Eastern Ontario (CHEO).

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