

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr GEN-CLOZAPINE

Clozapine Tablets Clozapine Orally Disintegrating Tablets

Read this carefully before you start taking **GEN-CLOZAPINE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **GEN-CLOZAPINE**.

Serious Warnings and Precautions

- **Severe neutropenia (Agranulocytosis)** (decrease in white blood cells): GEN-CLOZAPINE can cause a life-threatening decrease in your white blood cell count, which can lead to serious infection and death. Due to this risk, you must undergo regular blood testing if you are taking GEN-CLOZAPINE. Your healthcare professional will enroll you in a monitoring system to make sure your blood tests are done regularly (see **What is GEN-CLOZAPINE used for** and **Other warnings you should know about** for more information).
- **Heart problems:** Myocarditis (inflammation of the heart muscle) and cardiomyopathy (heart muscle disease) have occurred in people using GEN-CLOZAPINE. These reactions can be fatal. If you think you are experiencing a problem with your heart, get medical help **right away** (see the **Serious side effects and what to do about them** table below for a list of symptoms).
- **There** is a higher risk of death when medicines like GEN-CLOZAPINE are used in elderly patients with dementia. **GEN-CLOZAPINE is not for use in elderly patients with dementia.**

What is GEN-CLOZAPINE used for?

GEN-CLOZAPINE is a drug for the treatment of symptoms of schizophrenia. It is used in adults over 18 years of age who do not respond to, or who experience serious side-effects with other drugs used for the same purpose.

Important Information:

GEN-CLOZAPINE is only available through a distribution system.

Why does my healthcare professional need my consent?

Clozapine is available from many different suppliers and each supplier has a different monitoring system to ensure patient safety. If your healthcare professional and/or pharmacist (with your healthcare professional's approval) change the brand of clozapine you are taking, you will be moved to that supplier's monitoring system. Your healthcare professional needs your consent so that your supplier can:

- Access your past white blood cell count results from other suppliers
- See if you have experienced a decrease in your white blood cell count in the past while taking clozapine

Why is personal information such as my initials, birth date, gender and health card number being collected and used for identification purposes?

Since this information is specific to you, it helps to ensure that your test results are not mixed up with those of another person. Using this information also avoids the need to use your full name, which protects your privacy.

Can my personal information be used for other purposes?

No. Your information will only be used to make sure that you are properly monitored while using any brand of clozapine.

Where can I find information on the protection of health-related personal information in the private sector?

Information on this topic can be found on the website of Industry Canada, at the following address: <https://www.priv.gc.ca/en/privacy-topics/privacy-laws-in-canada/the-personal-information-protection-and-electronic-documents-act-pipeda/>

How does GEN-CLOZAPINE work?

GEN-CLOZAPINE belongs to a group of medicines called antipsychotic drugs. Antipsychotic medications affect dopamine and serotonin (chemicals found in the brain) that allow for the communication between your nerve cells. Exactly how this medication works is not known. However, it seems that GEN-CLOZAPINE improves the balance of dopamine and serotonin in your body.

What are the ingredients in GEN-CLOZAPINE?

Medicinal ingredients: clozapine

Non-medicinal ingredients:

Tablets: colloidal silicon dioxide, corn starch, lactose monohydrate, magnesium stearate, povidone and talc.

Orally disintegrating tablets: aspartame (phenylalanine*), cellulose microcrystalline, crospovidone, FD&C Yellow #6, magnesium stearate, mannitol, peppermint flavor (natural flavorings, maize maltodextrin, INS 1450 modified corn starch & moisture), silicon dioxide, sodium stearyl fumarate.

* The orally disintegrating tablets (ODT) contain phenylalanine (a component of aspartame). Each ODT strength contains the following amount of phenylalanine:

- 12.5 mg ODT: 0.73 mg phenylalanine
- 25 mg ODT: 1.45 mg phenylalanine
- 50 mg ODT: 2.90 mg phenylalanine
- 100 mg ODT: 5.80 mg phenylalanine
- 200 mg ODT: 11.61 mg phenylalanine

GEN-CLOZAPINE comes in the following dosage forms:

Tablets; 25 mg, 50 mg, 100 mg and 200 mg

Orally disintegrating tablets; 12.5 mg, 25 mg, 50 mg, 100 mg and 200 mg

Do not use GEN-CLOZAPINE if:

- You are allergic to clozapine or to any of the other ingredients listed in “**What are the ingredients in GEN-CLOZAPINE**”.
- You are unable to undergo regular blood tests

- You have ever had a low number of white blood cells, except if this was following a treatment for cancer (chemotherapy)
- You have or have ever had bone marrow disease or are taking medication to suppress bone marrow function
- You have or have ever had a disease that affect your blood cell formation
- You have liver disease
- You have kidney disease or kidney failure
- You have heart problems such as myocarditis, cardiomyopathy, or heart failure
- You have severe nervous system depression
- You have uncontrolled seizures
- You have or have ever had a “paralytic ileus”, severe constipation, an obstruction of the bowel or any other condition which has affected your large bowel

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take GEN-CLOZAPINE. Talk about any health conditions or problems you may have, including if you:

- Have a condition called phenylketonuria (an inherited disorder that increases the levels of a substance called phenylalanine in the blood) as the orally disintegrating tablets contain aspartame, a source of phenylalanine
- Have a fever or an infection
- Suffer from enlargement of the prostate
- Have a history of seizures (e.g., epilepsy)
- Have glaucoma (an eye condition)
- Have or have a family history of diabetes
- Have risk factors for developing blood clots such as:
 - a family history of blood clots
 - being over the age of 65
 - smoking
 - being overweight
 - having a recent major surgery (such as hip or knee replacement)
 - not being able to move due to air travel or other reasons
 - taking oral birth control (“The Pill”)
- Have a history of colon disease or lower abdominal surgery
- You have stable pre-existing liver disorder
- Have heart disease or family history of abnormal conduction in the heart called “prolongation of the QT interval”
- Have low blood pressure
- Have a fast heart rate (tachycardia)
- Have had a stroke
- Have or have had lung disease
- Have Alzheimer's disease
- Have a condition called dementia
- Are pregnant or planning to become pregnant
- Are breast-feeding or planning to breast-feed, you should not breast-feed if you are taking GEN-CLOZAPINE
- Have a history of or are at risk of sleep apnea (a sleep disorder where your breathing is interrupted during sleep)
- Are at risk for aspiration pneumonia

Tell your healthcare professional or pharmacist what your coffee intake is and if you smoke.

Abrupt changes in your habits may change the effect of GEN-CLOZAPINE.

Other warnings you should know about:

Effects on Newborns: In some cases, babies born to a mother taking GEN-CLOZAPINE during pregnancy may have symptoms that are severe and require the newborn to go to the hospital. Sometimes, the symptoms may resolve on their own. Get emergency medical help for your newborn, if they:

- Have trouble breathing
- Are overly sleepy
- Have muscle stiffness or floppy muscles (like a rag doll)
- Are shaking
- Are having difficulty feeding

Falls: GEN-CLOZAPINE can cause you to feel sleepy or dizzy and can affect your balance. This increases your risk of falling, which can cause fractures or other fall related-injuries, especially if you:

- Take sedatives
- Consume alcohol
- Are elderly
- Have a condition that causes weakness or frailty

Monitoring and Tests: Your healthcare professional will do tests before you start treatment with GEN-CLOZAPINE and while you are taking it. These tests may include:

- Blood tests to monitor:
 - White blood cell count
 - Blood sugar (glucose) levels in your body
 - Fat (lipid) levels in your body
 - Liver function
- Tests to monitor body weight as GEN-CLOZAPINE may cause you to gain weight

Why is the testing of your blood by your healthcare professional necessary?

In rare cases, GEN-CLOZAPINE can cause a life-threatening decrease of white blood cells. To ensure that your body has enough white blood cells, it is important to have regular blood testing done.

Blood testing must be done:

- Weekly during the first 26 weeks of treatment with clozapine. The risk for developing a deficiency of white blood cells is highest during this time.
- Following this initial period, you and your healthcare professional will evaluate the possibility of doing your blood tests to two-week intervals for the next 26 weeks.
- Following 52 weeks of continuous therapy, blood tests could be performed every 4 weeks if your clinical condition permits it.

Regular blood testing must be done for as long as you are taking GEN-CLOZAPINE.

Tell your healthcare professional immediately at the first signs of a cold, flu-like symptoms, fever, sore throat, weakness, or any other signs of infection. Your healthcare professional may check your blood cell count and take further measures if necessary.

Driving and using machines: Due to the risk of convulsions during GEN-CLOZAPINE treatment, you should avoid activities where a sudden loss of consciousness could cause risk to

yourself or others (e.g., driving, using machines, swimming, climbing).

GEN-CLOZAPINE can cause serious side effects including:

- Neuroleptic Malignant Syndrome (NMS) a condition that affects the nervous system
- Tardive Dyskinesia (TD) a condition that affects your movements that may be irreversible
- Severe skin reactions that can be life-threatening such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP)

See the **Serious side effects and what to do about them** table below for more information on these and other serious side effects.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with GEN-CLOZAPINE:

- Carbamazepine
- Phenytoin
- Omeprazole
- Rifampicin
- Erythromycin
- Cimetidine
- Valproic acid
- Medicines used to treat fungal infections such as fluconazole, miconazole, clotrimazole
- Medicines use to treat depression such as fluvoxamine, paroxetine, sertraline, fluoxetine, citalopram
- Ciprofloxacin
- Caffeine
- Tobacco smoking
- Narcotics
- Benzodiazepines
- Norepinephrine
- Epinephrine
- MAO (monoamine oxidase) inhibitors
- Any drugs used to suppress bone marrow function
- Oral birth control medicines
- Medicines used to treat high blood pressure
- Medicines used to treat allergies
- Medicines used to treat psychotic disorders
- Medicines that cause constipation
- Medicines called “anticholinergic agents”
- Alcohol

How to take GEN-CLOZAPINE:

- Take exactly as your healthcare professional has told you to
- If you think your dose is too weak or too strong, talk to your healthcare professional
- Try to take GEN-CLOZAPINE at the same time each day, this will help you remember to take your medicine

Tablets:

- Tablets can be taken whole or crushed.

Orally disintegrating tablets:

- Place on the tongue and swallow with saliva. May be chewed.
- No water is needed to take the orally disintegrating tablets.

Usual dose:

The usual starting dose is 12.5 mg (one-half of a 25 mg tablet or one 12.5 mg orally disintegrating tablet) once or twice on the first day. Your healthcare professional will then slowly increase your dose depending on how severe your disease is and how well your body tolerates the medicine. Your healthcare professional will decide the best dose for you. Take GEN-CLOZAPINE exactly as your healthcare professional has told you to.

Do not stop taking GEN-CLOZAPINE suddenly as it may cause unwanted side effects. If you need to stop taking GEN-CLOZAPINE, discuss with your healthcare professional how to slowly stop the medication.

Overdose:

If you think you, or a person you are caring for, have taken too much GEN-CLOZAPINE, contact a healthcare professional, hospital emergency department or regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose of GEN-CLOZAPINE, and remember within two hours, take the dose right away. Otherwise, skip the missed dose and continue with your regular dosing schedule. Do not take double doses. If you stop taking GEN-CLOZAPINE for more than two days, contact your healthcare professional for dosing instructions, do not re-start taking the drug.

What are possible side effects from using GEN-CLOZAPINE?

These are not all the possible side effects you may have when taking GEN-CLOZAPINE. If you experience any side effects not listed here, contact your healthcare professional.

- Headache
- Fever
- Confusion
- Drowsiness or feeling sleepy
- Dizziness
- Blurred vision
- Lightheadedness or fainting
- Falls and fractures
- Stuffy nose
- Increased saliva
- Dry mouth
- Trouble swallowing
- Sweating
- Heartburn
- Stomach pain

- Nausea
- Vomiting
- Constipation
- Diarrhea
- Weight gain
- Urinating less
- Nighttime bedwetting
- Abnormal ejaculation (dry orgasm)
- Stuttering or slurred speech
- Obsessive thoughts and behaviours
- Having trouble reading
- Uncontrolled bending of the body to one side
- Feeling restless or not being able to stay still
- Muscle weakness, stiffness or pain
- Joint pain
- Swelling of the cheeks
- Rash on the body or face
- Itchy skin
- Patches of skin discolouration

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
New or worsening constipation		✓	
COMMON			
Eosinophilia (increased numbers of certain white blood cells): abdominal pain, rash, weight loss, wheezing.		✓	
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up).		✓	
Neuroleptic Malignant Syndrome (NMS): pronounced muscle stiffness or inflexibility with high fever, rapid or irregular heartbeat, sweating, state of confusion or reduced consciousness.			✓
Seizures: uncontrollable shaking with or without loss of consciousness.			✓
Sudden weakness or numbness of the face, arms or legs and speech or vision problems.			✓
UNCOMMON			
Myocardial infarction (heart attack): pressure or squeezing pain between the shoulder blades, in the chest, jaw, left arm or upper abdomen, shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint and possible irregular heartbeat.			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Signs of infection: fever, severe chills, sore throat or mouth ulcers (sign of decreased white blood cells), nausea, vomiting, diarrhea, generally feeling unwell.		✓	
Tardive Dyskinesia (TD): muscle twitching or unusual/abnormal movement of the face or tongue or other parts of your body.		✓	
RARE			
Anemia (low level of red blood cells): fatigue, pale skin, headache, shortness of breath, dizziness, weakness, difficulty sleeping.		✓	
Diabetes (high sugar levels in the blood): Excessive thirst or eating, dry mouth and passing large amounts of urine, unexplained weight loss, poor wound healing, infections.		✓	
Dysphagia: difficulty swallowing that can cause food or liquid to get into your lungs, problems with your esophagus.		✓	
Heart Problems – Myocarditis and/or Pericarditis, Cardiomyopathy (inflammation of the heart muscle and/or lining around the heart; heart muscle disease): abnormal heartbeat, chest pain that may resemble a heart attack, fatigue, fever and other signs of infection including headache, muscle aches, sore throat, diarrhea, or rashes, joint pain or swelling, leg swelling, shortness of breath.		✓	
Liver Disorder: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite.	✓		
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid heartbeat, nausea, vomiting, tenderness when touching the abdomen.		✓	
Signs of respiratory tract infection or pneumonia such as fever, coughing, difficulty breathing or wheezing.		✓	
Venous thromboembolism (blood clot in a vein or artery): pain, tenderness or swelling in your arm or leg, skin that is red or warm, coldness, tingling or numbness, pale skin, muscle pain or spasms, weakness.		✓	
VERY RARE			
Allergic reaction: difficulty swallowing or breathing, wheezing, feeling sick to your stomach and throwing up, hives or rash, swelling of the face, lips, tongue or throat.			✓
Fast and irregular heartbeat that persists when you are at rest, possibly with shortness of breath and swelling of the feet or legs.		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Feeling sick, vomiting with severe/prolonged constipation		✓	
Hyperglycemia (high blood sugar): confusion, nausea, vomiting, excessive thirst or eating, excessive urination, abdominal pain, headache, blurred vision, fatigue.		✓	
Increased liver enzymes in the blood: dark urine, fatigue, loss of appetite, yellowing of the skin or eyes.		✓	
Nephritis (inflammation of the kidney): pelvic pain, pain or burning while urinating, frequent need to urinate, cloudy urine, blood or pus in the urine. Swelling especially face or legs.			✓
Priapism: Long-lasting (greater than 4 hours in duration) and usually painful erection of the penis.			✓
Severe skin reactions: fever, severe rash, swollen lymph glands, flu-like feeling, blisters and peeling skin that may start in and around the mouth, nose, eyes and genitals and spread to other areas of the body, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine			✓
Thrombocytopenia (low blood platelets): bruising or bleeding for longer than usual if you hurt yourself, fatigue and weakness.		✓	
Thrombocytosis (high blood platelets); headache, dizziness or lightheadedness, chest pain, weakness, fainting, temporary vision change, numbness or tingling of the hands and feet.	✓		

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at room temperature (between 15°C and 30°C). Protect from heat.

Store in original container.

Do not use after the expiry date shown on the bottle.

Keep out of the reach and sight of children.

If you want more information about GEN-CLOZAPINE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.mylan.ca, or by calling 1-844-596-9526.



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Mylan Pharmaceuticals ULC
Etobicoke, ON M8Z 2S6
1-844-596-9526
www.mylan.ca