

NEW ZEALAND CONSUMER MEDICINE INFORMATION

CLOZARIL®

Clozapine tablets 25 mg and 100 mg



What is in this leaflet

Please read this leaflet carefully before you start taking Clozaril

This leaflet answers some common questions about Clozaril.

It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

The information in this leaflet was last updated on the date listed on the final page. More recent information on the medicine may be available.

You should ensure that you speak to your pharmacist or doctor to obtain the most up to date information on the medicine. You can also download the most up-to-date leaflet from www.medsafe.govt.nz

Those updates may contain important information about the medicine and its use of which you should be aware.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking Clozaril against the benefits they expect it will provide.

If you have any concerns about taking this medicine, ask your doctor or pharmacist.

Keep this leaflet with the medicine. You may need to read it again.

What Clozaril is used for

Clozaril is used to treat schizophrenia, which is a mental illness involving disturbances in thinking, feelings and behaviour. It

helps to correct chemical imbalances in the brain which may cause mental illness.

Clozaril is only used to treat patients suffering with schizophrenia when other antipsychotic medicines either have not worked or have caused severe side effects.

This medicine contains an active ingredient called clozapine. Clozaril tablets belong to a group of medicines called antipsychotics.

Your doctor may have prescribed it for another reason.

Ask your doctor if you have any questions about why Clozaril has been prescribed for you.

Clozaril is available only with a doctor's prescription.

There is no evidence that it is addictive.

Clozaril is not recommended for use in children or adolescents, as there is not enough information on its use in that age group.

Clozaril is also not recommended for patients aged 60 years and over with dementia as there is not enough information.

Before you take Clozaril

When you must not take it

Do not take Clozaril if you have an allergy to:

- any medicine containing-clozapine
- any of the ingredients listed at the end of this leaflet.

Some of the symptoms of an allergic reaction may include shortness of breath, wheezing or

difficulty breathing; swelling of the face, mouth and throat, as well as the tongue, which may be itchy or painful; swelling of other parts of the body; rash, itching or hives on the skin.

If you think that you are allergic to Clozaril, ask your doctor for advice before taking this medicine.

Do not take Clozaril if you have a low white blood cell count or have previously had a low white blood cell count caused by a medicine (except if it was following a treatment for cancer).

Clozaril can cause agranulocytosis (a condition with a reduced number of white blood cells). These cells are needed to fight infections. If you have a low white blood cell count or have had one in the past, you must not take Clozaril.

Do not take Clozaril if you are unable to have regular blood tests.

Before starting this medicine and during your therapy, checks will be required to monitor the levels of various components in your blood. Your doctor will tell you when these tests are needed.

Do not take Clozaril if you have any of the following medical conditions:

- any disease of the blood which causes a reduced number of blood cells or platelets
- bone marrow disease
- symptoms of active liver disease such as jaundice (yellow colour to the skin and eyes, feeling sick, loss of appetite) or any other severe liver disease
- severe kidney disease
- myocarditis (an inflammation of the heart muscle) or any other heart problems

- uncontrolled epilepsy (i.e. you still have some seizures)
 - paralytic ileus, a condition in which the small bowel does not work properly
 - severe constipation, obstruction of the bowel, or any other condition which has affected your large bowel
 - problems with alcohol or drug abuse
 - circulatory collapse.
- puckering of the mouth or chewing movements)
 - problems with your liver or kidneys
 - glaucoma, a condition in which there is usually a build-up of fluid in the eye
 - enlargement of the prostate or prostate problems
 - epilepsy that is under control (i.e. you no longer have seizures)
 - drowsiness, fainting, muscle weakness, which may lead to falls
 - diabetes or a family history of diabetes
 - chronic constipation or abdominal pain.
 - taking medication that can cause constipation
 - if you have had a stroke in the past.
 - dementia, a condition in which there is a decline in all areas of mental ability
 - Parkinson's disease
 - any other serious medical condition.

Clozaril must not be given to anyone who is unconscious or in a coma, or who has an acute mental illness caused by alcohol or drugs.

Do not take this medicine after the expiry date printed on the pack or if the packaging is torn or shows signs of tampering. If it has expired or is damaged, return it to your pharmacist for disposal.

If you are not sure whether you should start taking Clozaril, talk to your doctor or pharmacist.

Before you start to take it

Tell your doctor if you have allergies to other medicines or to any other substances such as foods, preservatives or dyes.

Tell your doctor if you have ever had any of the following medical conditions:

- any previously occurred side effects while taking clozapine.
- any form of heart disease or a family history of heart disease
- family history of an abnormal conduction in the heart called "prolongation of the QT interval"
- history of neuroleptic malignant syndrome, a reaction to some medicines with a sudden increase in body temperature, sweating, fast heartbeat, muscle stiffness and fluctuating blood pressure, which may lead to coma
- tardive dyskinesia, a reaction to some medicines with uncontrolled movements of the tongue, face, mouth or jaw (such as puffing of the cheeks,

Tell your doctor if you are pregnant or plan to become pregnant.

Experience with Clozaril in pregnancy is very limited. If you need to take this medicine during pregnancy, your doctor will discuss with you the benefits and risks involved.

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.

If you start taking Clozaril, make sure you use a contraceptive to prevent pregnancy.

Tell your doctor if you are breast-feeding or plan to breast-feed. You should not breast feed during Clozaril treatment. This medicine may pass into breast milk and may affect your baby.

Tell your doctor if you smoke and how much coffee you drink.

Sudden changes in your usual smoking or coffee drinking habits can also change the effects of Clozaril.

Tell your doctor how much alcohol you drink, as it can worsen the side effects of Clozaril. **You should not drink alcohol while you are taking Clozaril**

Tell your doctor if you will be in a hot environment or you do a lot of vigorous exercise. Clozaril may make you sweat less, causing your body to overheat.

Tell your doctor if you are lactose intolerant.

This medicine contains lactose.

If you have not told your doctor about any of the above, tell them before you start taking Clozaril.

Taking other medicines

Tell your doctor or pharmacist if you are taking any other medicines, including any that you get without a prescription from your pharmacy, supermarket or health food shop.

You should also tell any health professional who is prescribing a new medication for you that you are taking Clozaril.

Some medicines and Clozaril may interfere with each other. These include:

- medicines that decrease the number of blood cells produced by your body
- other antipsychotic medicines used to treat mental illnesses
- medicines used to control depression or mood swings such as lithium, paroxetine, sertraline, fluoxetine, citalopram, MAO inhibitors, perazine, fluvoxamine
- benzodiazepines and other medicines used to treat anxiety or to help you sleep
- medicines used to control epilepsy, including phenytoin, carbamazepine and valproic acid

- warfarin, a medicine used to prevent blood clots
- strong pain killers (also known as narcotics) such as morphine
- St John's wort, (hypericum) an ingredient in many medicines that you can buy without a prescription from a pharmacy, health food shop or supermarket
- antihistamines, medicines used for colds or allergies such as hay fever
- anticholinergic medicines, which are used to relieve stomach cramps, spasms and travel sickness
- medicines used to treat Parkinson's disease
- medicines used to treat high blood pressure
- digoxin, a medicine used to treat heart problems
- medicines used to treat a fast or irregular heart beat
- some medicines used to treat stomach ulcers, including cimetidine and omeprazole
- some antibiotic medicines, including erythromycin, ciprofloxacin and rifampicin
- some medicines used to treat fungal or viral infections
- nicotine in medicines used to help you quit smoking, such as nicotine patches or chewing gum
- atropine, a medicine which may be used in some eye drops or cough and cold preparations
- adrenaline, a drug used in emergency situations
- medicines that contain caffeine or alcohol
- birth-control tablets.

These medicines may be affected by Clozaril or they may affect how well Clozaril works. You may need to take different amounts of your medicines or you may need to take different medicines.

Your doctor and pharmacist have more information on medicines to be careful with or avoid while taking this medicine.

How to take Clozaril

Follow all directions given to you by your doctor and pharmacist carefully. They may differ from the information contained in this leaflet.

If you do not understand the instructions on the label, ask your doctor or pharmacist for help.

How much to take

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

The usual starting dose is half of a 25 mg tablet once or twice on the first day. The dose is usually increased to one 25 mg tablet once or twice on the second day. After that the dose can be slowly increased until the desired effect is achieved. Usually the total amount of Clozaril needed each day will be between 200 mg and 450 mg but some people will take a dose outside this range depending on their needs.

Do not exceed the prescribed dose. If you think the dose is too weak or too strong, talk to your doctor. Some people may require doses of up to a maximum of 900 mg/day.

Once the maximum benefit is reached, the dose can often be decreased as recommended by your doctor to suit your medical needs.

If you have heart, kidney or liver disease, are prone to seizures (fits) or are elderly, your doctor may start you on a lower dose and increase it more gradually to prevent unwanted side effects.

How to take it &

Swallow the tablets with a full glass of water or other liquid.

When to take it

Take your medicine at about the same time each day. Taking your tablets at the same time each day will have the best effect. It will also help you remember when to take

them.

The total daily amount of Clozaril is usually divided into 2 doses (morning and bedtime). But, if your total dose is 200 mg or less, your doctor may allow you to take the whole amount at once, usually in the evening.

How long to take it

Continue taking your medicine for as long as your doctor tells you. This medicine helps to control your condition but does not cure it. It is important to keep taking your medicine even if you feel well.

Your doctor will check your progress to make sure the medicine is working and will discuss with you how long your treatment should continue.

If you have any concerns, talk to your doctor or pharmacist.

If you forget to take it

If it is almost time for your next dose (4 hours or less to the next dose), skip the dose you missed and take the next dose when you are meant to.

Otherwise, take it as soon as you remember, and then go back to taking it as you would normally.

Do not take a double dose to make up for the one that you missed. This may increase the chance of you getting an unwanted side effect.

If you have forgotten to take Clozaril for more than 2 days, do not start taking it again before you contact your doctor.

To prevent unwanted side effects, your doctor will probably want you to restart Clozaril at a low dose and increase it gradually back to the amount you were taking before.

If you are not sure what to do, ask your doctor or pharmacist.

If you have trouble remembering when to take your medicine, ask your pharmacist for some hints.

While you are taking Clozaril

Things you must do

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

You must have strict and regular blood tests while taking Clozaril. Clozaril can cause agranulocytosis. This is a condition where the number of white blood cells in your body is reduced. White blood cells are needed to fight infection.

There is no way of knowing who is at risk of developing agranulocytosis.

Deaths have occurred in severe cases of agranulocytosis. However, with regular blood tests, the problem can be detected early. If Clozaril is stopped as soon as possible, the white blood cell numbers should return to normal.

You must have a blood test at least once a week for the first 18 weeks after starting Clozaril.

This is the time when the risk of agranulocytosis is greatest. These tests can tell the doctor whether the white blood cell count is dropping.

After 18 weeks, you must have a blood test at least every 4 weeks for as long as you are taking Clozaril and for a month after stopping the medicine.

There are some situations where you may need to have blood tests more often (e.g. twice a week). Your doctor will explain this to you.

If the number of white blood cells falls below a critical level, Clozaril will be stopped immediately and you must never take Clozaril again.

If you suffer from high level of sugar in the blood (diabetes) your doctor may regularly check your level of sugar in the blood.

Watch for important side effects. If you develop a fast or irregular

heartbeat that is present even when you are resting, accompanied by rapid breathing, shortness of breath, swelling of the feet or legs, dizziness or light headedness, or chest pain, contact your doctor immediately as these symptoms may lead to death.

These symptoms could be signs of myocarditis, an inflammation of the heart muscle, or another heart condition. Your doctor may want to refer you to a cardiologist for further tests.

If you develop a fever, rigid muscle, excessive sweating or fast heart rate contact your doctor immediately.

Some patients develop a fever in the first few weeks of taking Clozaril. You must be checked carefully to make sure that you do not have agranulocytosis, myocarditis or neuroleptic malignant syndrome, a reaction to some medicines with a sudden increase in body temperature.

If you develop a sore throat, mouth ulcers, flu-like symptoms or any other sign of a cold or infection, contact your doctor immediately.

Your doctor will check your blood to decide if your symptoms are an early sign of agranulocytosis. Flu-like symptoms may also be a sign of myocarditis.

If you notice any uncontrolled movements of the tongue, face, mouth or jaw, such as puffing of the cheeks, puckering of the mouth or chewing movements, tell your doctor immediately.

These are symptoms of a very rare condition called tardive dyskinesia which may develop in people taking antipsychotic medicines. This condition is more likely to happen during long-term treatment, especially in elderly women. In very rare cases, it may be permanent. However, if detected early, these symptoms are usually reversible.

Make sure you use a contraceptive to prevent pregnancy during treatment with Clozaril.

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.

If you suffer from abdominal pain and constipation tell your doctor immediately. These may be a sign of abnormal dilation of the large intestines which may lead to death.

If you develop abdominal pain it could be a sign of breakdown of part of the intestine due to reduced blood supply which may lead to death.

If you become pregnant while taking this medicine, tell your doctor immediately.

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.

Your doctor can discuss with you the risks of taking it while you are pregnant.

If you are about to be started on any new medicine, remind your doctor and pharmacist that you are taking Clozaril.

Tell any other doctor, dentist or pharmacist who treats you that you are taking Clozaril.

If you are going to have surgery, tell the surgeon or anaesthetist that you are taking this medicine. It may affect other medicines used during surgery.

Things you must not do

Do not take Clozaril to treat any other complaints unless your doctor tells you to.

Do not give this medicine to anyone else, even if their condition seems similar to yours.

You should not drink alcohol while you are taking Clozaril.

Clozaril may enhance the effects of alcohol.

Do not stop taking Clozaril or lower the dosage, even if you are feeling better, without checking with your doctor.

If you stop taking Clozaril suddenly, your condition may worsen or you may have unwanted side effects such as excessive sweating, headache, nausea (feeling sick), vomiting and diarrhoea.

If this medicine is stopped for any reason, your doctor will reduce the dose gradually, over a one to two week period, to avoid side effects, before stopping the medicine completely.

Do not let yourself run out of Clozaril over the weekend or holidays.

Things to be careful of

Be careful driving or operating machinery, or anything else that could be dangerous until you know how Clozaril affects you.

As with other antipsychotic medicines, Clozaril may cause tiredness, drowsiness, dizziness, light-headedness, fainting or seizures (fits) in some people. If you have any of these symptoms, do not drive, operate machinery or do any tasks where you need to be alert.

Be careful when taking pain relievers, sleeping tablets or antihistamines (medicines for colds or allergies such as hay fever) while you are taking Clozaril.

Clozaril can increase the drowsiness caused by medicines that affect your nervous system.

If you feel light-headed, dizzy or faint, be careful when getting up from a sitting or lying position.

Clozaril may lower your blood pressure, especially at the start of treatment. These symptoms can usually be prevented by getting up slowly, and flexing leg muscles and toes to get the blood flowing. When getting out of bed, dangle your legs over the side for a minute or two before standing up. If this problem continues or gets worse, talk to your doctor.

Inform your doctor if you stop smoking or change the number of caffeine-containing drinks that you have in one day.

These changes can affect the levels of this medicine in your blood.

Clozaril may cause alteration in blood lipids. It may also cause weight gain. Your doctor may monitor your weight and blood lipid levels.

Clozaril can cause sleepiness, and remaining in bed for prolonged duration in combination with weight gain may lead to the formation of blood clots in some patients.

Make sure you keep cool in hot weather and keep warm in cool weather.

As with other antipsychotic medicines, Clozaril may affect the way your body reacts to temperature changes. It may prevent sweating, even during heatwaves. You may feel dizzy or faint if you are too hot.

To stay cool in hot weather, try to do the following:

- wear light clothing
- spend time in air-conditioned environments (or keep windows open and use electric fans)
- drink plenty of water
- take cool baths or showers and avoid hot baths and saunas
- try to restrict exercise or heavy work to cool parts of the day.

In case of overdose

If you take too much (overdose)

Immediately telephone your doctor or the National Poisons Information Centre (0800 POISON or 0800 764 766) for advice, or go to Accident and Emergency at the nearest hospital, if you think that you or anyone else may have taken too much Clozaril. Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention.

Symptoms of an overdose may include light headedness due to low blood pressure, too much saliva, difficulty breathing, fast or irregular heartbeat, drowsiness, confusion and unconsciousness.

Side effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking Clozaril, even if you do not think it is connected with the medicine.

This medicine helps most people with schizophrenia, but it may have unwanted side effects in some people.

All medicines can have side effects. Sometimes they are serious, but most of the time they are not. You may need medical treatment if you get some of the side effects.

If you are over 60 years old, you should be especially careful while taking this medicine. Report any side effects promptly to your doctor.

You may be more likely to get some of the side effects of Clozaril, such as rapid heartbeat, dizziness or light-headedness due to low blood pressure, constipation and difficulty urinating.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor or pharmacist if you notice any of the following and they worry you:

- tiredness, drowsiness,
- dizziness or light headedness when standing up
- unexplained tiredness
- headache
- agitation
- confusion
- disorientation
- vivid dreams
- dry mouth
- increased or decreased sweating
- diarrhoea
- too much saliva
- stomach discomfort, especially after a meal
- heartburn
- difficulty in swallowing

- weight gain, especially excessive weight gain.
- changes in sexual function
- painful menstrual periods
- repetitive and ritualised behaviour (obsessive compulsive symptoms)
- excessive urination
- problems in passing or holding urine
- stuttering in speech or difficulty speaking.
- stuffy nose
- obsessive thoughts
- swelling of the glands in the cheeks
- nocturnal bedwetting
- rash, purplish-red spots, fever or itching
- a strong urge to move the legs (restless legs syndrome) with an unpleasant feeling in the legs.
- muscle weakness

Tell your doctor as soon as possible if you notice any of the following:

- constipation or fewer bowel movements than normal (if it seems to be getting worse, check with your doctor immediately)
- hard or dry stools, or difficulty passing gas
- abdominal pain (if it seems to be getting worse, check with your doctor immediately)
- diarrhoea (that may be bloody) with abdominal pain and fever
- nausea (feeling sick),
- vomiting
- dark urine
- change in skin colour
- "butterfly" facial rash, joint pain, muscle pain, fever and fatigue
- skin reactions
- sudden, uncontrollable increase in blood pressure
- uncontrolled bending of the body to one side
- for males, dry orgasm (retrograde ejaculation) where very little or no semen is ejaculated as it enters the bladder instead. Urine will appear cloudy after an orgasm
- blurred vision, difficulty in reading

The above list includes serious side effects that may require medical attention.

If any of the following happen, tell your doctor immediately or go to Accident and Emergency at your nearest hospital:

- falls due to seizures, drowsiness, fainting, muscle weakness.
- fainting or loss of consciousness
- crushing chest pain/chest pain
- fever, sore throat, mouth ulcers, "flu-like" symptoms (chills, aching joints, swollen glands, lack of energy) or any other signs of infection
- a fast or irregular heartbeat (palpitations) that is present even when you are resting, may be accompanied by rapid breathing, shortness of breath, swelling of the feet or legs, dizziness or light headedness, or chest pain
- sudden signs of allergy such as rash, itching or hives on the skin; swelling of the face, lips, tongue or other parts of the body; wheezing or troubled breathing
- symptoms of neuroleptic malignant syndrome, with a sudden increase in body temperature, sweating, fast heartbeat, muscle stiffness and fluctuating blood pressure, which may lead to coma
- seizures (fits)
- pain in the stomach, often accompanied by nausea and vomiting
- severe/prolonged constipation, which may be accompanied by abdominal pain,
- bloating or belly swelling
- signs of loss of blood sugar control such as excessive thirst, drinking or eating large amounts, weakness, passing large amounts of urine, dry mouth and skin
- spontaneous bleeding, or bruising more easily than normal
- signs that blood clots may have formed, such as sudden severe headache, sudden loss of coordination, blurred vision or sudden loss of vision,

slurred speech, numbness in an arm or leg

- yellowing of the skin and/or eyes, sometimes accompanied by feeling sick and loss of appetite, nausea, fever, itching, light coloured bowel motions or dark urine
- difficulty in passing urine or blood in the urine
- loss of bladder control
- muscle stiffness, muscle weakness, muscle spasms, or muscle pain
- rigidity or stiffness in the arms and legs
- shaking or tremor, feeling unable to sit still
- abnormal movements, inability to initiate movement, inability to remain motionless, inner feeling restless, stiff limbs, trembling hands
- symptoms of tardive dyskinesia (uncontrolled involuntary purposeful movements of the tongue, face, mouth or jaw such as puffing of the cheeks, puckering of the mouth, chewing movements, grimacing, lip-smacking, rapid eye blinking)
- persistent painful erection or prolonged erection
- signs of respiratory tract infection or pneumonia such as fever, coughing, difficulty breathing, wheezing
- signs of sepsis such as shivering, fever, rapid breathing and heart rate, a change in your mental state such as confusion or disorientation
- muscle spasms, fever, red-brown urine
- chest pain, cough, hiccups, rapid breathing
- varying degree of pain in the chest and abdomen.
- pauses in breathing or periods of shallow breathing (that may occur even when sleeping)
- signs of anaemia, such as tiredness, headaches, being short of breath, and looking pale
- severe skin rash with fever.

The above list are serious side effects that need medical attention.

Sudden unexplained death and

heart attacks that may lead to death have been reported with Clozaril.

Tell your doctor if you notice anything else that is making you feel unwell.

Other side effects not listed here may happen in some people. Tell your doctor if you notice any other effects.

Some of these side effects (for example, changes in cholesterol level or blood pressure, or changes in function of the liver, kidney, heart or brain) can only be found when your doctor does tests from time to time to check your progress.

Do not be alarmed by this list of possible side effects. You may not experience any of them.

After taking Clozaril

Storage

Keep your tablets in the original container until it is time to take them. If you take the tablets out of the original container they may not keep well.

Keep your tablets that come in a bottle in a cool dry place where the temperature stays below 25°C.

Keep your tablets that come in a blister in a cool dry place where the temperature stays below 30°C.

Do not store Clozaril or any other medicine in the bathroom or near a sink. Do not leave it on a window sill or in the car.

Heat and dampness can destroy some medicines.

Keep it where children cannot reach it.

A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines.

Disposal

If your doctor tells you to stop taking Clozaril or the expiry date has passed, ask your pharmacist what to do with any medicine that is left over.

Remember that you must still have your blood tested for a month after stopping this medicine.

Product description

What it looks like

Clozaril 25 mg: small, round, yellow tablets with a break line and LO on one side and SANDOZ on the other side; containers of 50 or 100 tablets.

Clozaril 100 mg: small, round, yellow tablets with a break line and ZA on one side and SANDOZ on the other side; containers of 50 or 100 tablets.

The quantity of tablets provided to you will be determined by your doctor.

Ingredients

Active ingredient:

Clozaril tablets contain 25 mg or 100 mg of clozapine.

Inactive ingredients:

Clozaril also contains:

- silica colloidal anhydrous
- talc-purified
- magnesium stearate
- lactose
- maize starch
- povidone

This medicine does not contain sucrose, gluten, tartrazine or any other azo dyes.

If you want to know more

Should you have any questions regarding this product, please contact your pharmacist or doctor.

Who supplies this medicine

Clozaril is supplied in New Zealand by:

Mylan New Zealand Ltd,
PO Box 11183,
Eilerslie,
Auckland
NEW ZEALAND.

Telephone: (09) 579 2792

Date of Information

10 August 2020 (Based on datasheet dated 10 August 2020).