CLOPINE®

Clozapine
25, 50, 100 and 200 mg tablets
50 mg/mL oral suspension

What is in this leaflet

Please read this leaflet carefully before you start taking CLOPINE.

This leaflet answers some common questions about CLOPINE. It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

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

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 CLOPINE is used for

CLOPINE tablets and suspension belong to the group of medicines known as antipsychotics. This group of medicines is mainly used in the treatment of schizophrenia. Schizophrenia is a mental illness with disturbances in thinking, feelings and behaviour.

This medicine is only used in patients with schizophrenia for whom other antipsychotic medicines have not worked or have caused severe side effects.

This medicine is thought to work by correcting the chemical imbalances in the brain, which may cause mental illness.

Your doctor may have prescribed it for another reason.

Ask your doctor if you have any questions about why this medicine has been prescribed for you. This medicine is available only with a doctor’s prescription.

There is no evidence that this medicine is addictive.

CLOPINE is not recommended for use in children or adolescents under the age of 16, as there is not enough information on its use in that age group.

Before you take CLOPINE

When you must not take it

Do not take this medicine if you have an allergy or have ever experienced an allergic reaction to the active ingredient, clozapine, or to any of the other ingredients listed at the end of this leaflet.

Symptoms of an allergic reaction to this medicine may include:

- breathing problems such as shortness of breath, wheezing, difficulty breathing
- skin rash, itching or hives
- swelling of the face, lips, tongue or other parts of the body

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

Do not take this medicine if you have a low white blood cell count, or if you have previously had a low white blood cell count caused by use of a medicine.

CLOPINE can cause agranulocytosis. With this condition, the number of white blood cells (which are needed to fight infections) is reduced. If you
have a low white blood cell count or have had one in the past, you must not take this medicine.

Do not take CLOPINE 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 CLOPINE if you have or have had any of the following medical conditions:

- any blood disorder that may lower your red blood cell or platelet count
- symptoms of active liver disease such as jaundice (yellowing of the skin and eyes, feeling sick, loss of appetite) or liver failure
- problems with your kidneys
- inflammation of heart muscle (myocarditis) or any other heart disorder
- uncontrolled epilepsy (fits or seizures)
- paralytic ileus, a small bowel condition any large bowel conditions, including severe constipation or obstruction
- bone marrow disorder
- acute mental illness caused by alcohol or another drug.

CLOPINE must not be given to anyone who is unconscious or in a coma.

Do not take this medicine if the expiry date (EXP) shown on the outer container, on the blister strip or on the bottle has passed. Do not use if the tablets or suspension show signs of deterioration or if the packaging shows signs of tampering.

If you take this medicine after the expiry date has passed, it may not work as well or you may feel unwell.

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

**Before you start to take it**

Tell your doctor if you have any allergies to:

- any other medicines
- any other substances such as foods, preservatives or dyes

Tell your doctor if you have or have had any medical conditions, especially the following:

- heart disease or a family history of heart disease or disorders
- chest pain
- neuroleptic malignant syndrome (NMS) - a reaction to some medicines with a sudden increase in body temperature, sweating, fast heart heartbeat, muscle stiffness and fluctuating blood pressure, which may lead to coma
- a condition called tardive dyskinesia characterised by uncontrollable twitching or jerking of the arms or legs
- diseases of liver or kidneys or family history of liver and kidney problems
- glaucoma (raised pressure in the eye)
- prostate problems especially in the elderly
- fits or epilepsy that is under control
- diabetes
- chronic constipation or abdominal pain
- stroke
- anticholinergic effects - confusion and excitement especially in the elderly
- any other medical condition

Your doctor may want to take special precautions if you have any of these conditions.

Tell your doctor if you are pregnant or are thinking of becoming pregnant during treatment with CLOPINE.

There is limited information on the safety of clozapine in pregnancy. Your doctor will discuss the risks and benefits of taking this medicine during pregnancy.

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

Tell your doctor if you are breast-feeding or plan to breast-feed.
It is recommended that you do not breast-feed while taking CLOPINE, as clozapine may pass into breast milk and therefore there is a possibility that the breast-fed baby may be affected.

**Tell your doctor if you smoke and how much coffee you drink.** Nicotine and coffee can affect the amount of clozapine in your body. Sudden changes in your usual smoking or coffee drinking habits can also change the effects of this medicine.

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

**Tell your doctor if you are lactose intolerant.** This medicine contains lactose.

### Taking other medicines

Tell your doctor or pharmacist if you are taking any other medicines, including any that you buy 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 CLOPINE.

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

- medicines that may decrease the number of blood cells produced by your body
- other medicines for schizophrenia, mental disorders, depression or mood swings
- sleep inducing medicines, such as benzodiazepines
- epilepsy medicines e.g. phenytoin, carbamazepine, valproic acid
- warfarin or heparin - medicines used to prevent blood clots
- strong pain killers e.g. morphine
- St John’s wort (Hypericum perforatum) - a herbal remedy
- antihistamines - medicines used to control and prevent symptoms of allergies such as hay fever
- anticholinergic medicines used to relieve stomach cramps, spasms and travel sickness
- Parkinson’s disease medicines
- high blood pressure medicines
- medicines used to treat a fast or irregular heart beat e.g. digoxin
- medicines used for stomach ulcers e.g. cimetidine, omeprazole
- medicines used to treat bacterial infections e.g. erythromycin, rifampicin
- medicines used to treat fungal and viral infections.
- nicotine in medicines used to help you quit smoking e.g. nicotine patches or chewing gum
- atropine - a medicine which may be used in some eye drops or cough preparations
- adrenaline - a drug used in emergency situations
- oral contraceptives (birth-control tablets)

These medicines may be affected by CLOPINE or may affect how well CLOPINE work. Your doctor will advise you.

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

### How to take CLOPINE

Your dose of CLOPINE has been determined for you by your doctor. The dose will depend on how you respond to the medicine, other medicines you are taking, and other medical conditions that you may have. The dose may be altered from time to time.

Carefully follow all directions given to you by your doctor. Their directions 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 determine the most appropriate dose for you.

**Take CLOPINE exactly as prescribed by your doctor.**

If you have heart, kidney or liver disease, epilepsy or you are elderly; your doctor may start you on a lower dose and gradually increase the dose to prevent unwanted effects.

**Do not take more or less CLOPINE than your doctor has prescribed.** If you think the dose is too weak or too strong, talk to your doctor.

**How to take it**

The total daily amount of CLOPINE is usually divided into two doses. However, if your total dose is 200 mg or less, your doctor may allow you to take the whole amount in one dose, usually in the evening.

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

CLOPINE suspension may be taken alone or in water if required.

**When to take it**

Take your medicine at about the same time each day.

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

It does not matter if you take this medicine before or after food.

**If you forget to take it**

If it is almost time for your next dose (within four hours), skip the dose you missed and take your next dose when you are meant to. Otherwise take it as soon as you remember, and then go back to taking your medicine as you would normally.

If you miss a dose of CLOPINE, do not take a double dose to make up for the missed dose. If you have stopped taking CLOPINE for more than two days, do not start taking it again before you contact your doctor.

To prevent unwanted side effects, your doctor will probably restart you on CLOPINE at a lower dose and increase it gradually back to your normal dose.

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

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

**How long to take it**

Take this medicine until your doctor tells you to stop. Your doctor will check your progress and decide how long to continue your treatment. 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.

Do not lower the dosage, even if you are feeling better, unless your doctor tells you to do so. Your condition may worsen if you suddenly stop taking it. Your doctor will gradually reduce the amount you take each day before stopping the medicine completely.

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

If you have any concerns, talk to your doctor.

**While you are taking CLOPINE**

**Things you must do**

You must have strict and regular blood tests while taking this medicine. This medicine can cause agranulocytosis. This is a condition where the number of white blood cells (which are necessary to fight infection in your body) may be reduced. Severe cases of agranulocytosis have resulted in deaths.
Only regular blood tests can tell the doctor if you are at risk of agranulocytosis. Therefore agranulocytosis can be detected early, and if this medicine is stopped as soon as possible, the white blood cell numbers should return to normal.

After starting on this medicine, you must have a blood test at least once a week for the first 18 weeks of treatment (this is when the risk of agranulocytosis is greatest), thereafter at least every 4 weeks for as long as you are taking this medicine, and for one month after stopping.

Your doctor will advise if blood tests are required more often. These tests will tell the doctor if the white blood cell count is dropping.

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

If the number of your white blood cells falls below a safe level, this medicine must be stopped immediately and you must never take any medicines containing clozapine again.

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

Contact your doctor immediately if:
- you develop a fast or irregular heart beat that is present even when you are resting, accompanied by rapid breathing, shortness of breath, dizziness or light headedness, or chest pain. These symptoms could be signs of myocarditis, an inflammation of the heart muscle, or another heart condition.
- you have muscle weakness, fever, fast or irregular heart beat and excessive sweating. These are symptoms of a very rare condition called Neuroleptic Malignant Syndrome (NMS) - a reaction to some medicines, which can cause a sudden increase in body temperature.
- you have uncontrolled movements of the tongue, jaw (such as puffing at the cheeks, chewing movements, puckering of the mouth), face and mouth. These are symptoms of a very rare condition called tardive dyskinesia - a condition more likely to happen during long term treatment, especially in older women.
- you develop a sore throat, mouth ulcers, fever, any "flu-like" symptoms such as swollen glands or other signs of infection as these symptoms may be an early sign of agranulocytosis. Flu-like symptoms may also be a sign of myocarditis.

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

Be sure to keep all of your doctor's appointments so that your progress can be checked.

Tell any other doctors, dentists, and pharmacists who are treating you that you are taking CLOPINE or if you are about to be started on any new medicines or if you plan to have surgery

Things you must not do

Do not give the medicine to anyone else even if their symptoms seem similar or they have the same condition as you.

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

You might get withdrawal reactions if you stop CLOPINE abruptly such as sweating, headache, nausea (feeling sick), vomiting (being sick) and diarrhoea. Those signs may be followed by more serious side effect so do not stop taking CLOPINE without asking your doctor.

Things to be careful of

Be careful driving or operating machinery until you know how this medicine affects you. You may feel tired, drowsy, dizzy or you may feel faint while taking this medicine, especially during the early stages of treatment. If you have any of these symptoms, do not drive, operate machinery or do any tasks where you need to be alert.
If the tablets or suspension make you feel dizzy, light-headed or faint, be careful when getting up from a sitting or lying position. This medicine may lower your blood pressure, especially at the start of treatment. Getting up slowly and flexing leg muscles and toes to get the blood circulating can usually prevent these symptoms. When getting out of bed, dangle your legs over the side for a minute or two before standing up.

Be careful when drinking alcohol or when taking antihistamines (medicines used for hay fever, allergies or colds), sleeping tablets or tablets to relieve pain while taking this medicine. Clozapine can increase drowsiness caused by alcohol and by medicines affecting your nervous system.

Clozapine may cause weight gain or affect your blood lipid levels. Your doctor may monitor your weight and blood lipid levels.

Clozapine may affect the way your body controls temperature, and it may prevent sweating even in very hot weather. Exercise, hot baths or saunas may make you feel dizzy or faint while you are taking this medicine.

In case of overdose

If you take too much (overdose)

Immediately telephone your doctor or the National Poisons Centre (telephone 0800 POISON or 0800 764 766), or go to accident and emergency at your nearest hospital, if you think that you or anyone else may have taken too much CLOPINE.

The most common signs and symptoms of clozapine overdose include: drowsiness, confusion and coma; light-headedness; shallow breathing or breathing more slowly; fast or irregular heartbeat and dribbling. Occasionally, fits have also been reported.

Side effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are using CLOPINE.

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

If you are over 60 years old, you may have an increased chance of getting side effects.

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

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

- tiredness and drowsiness
- dizziness, fainting, light-headedness, seizures
- constipation
- headache
- feeling anxious, vivid dreams, changes in behaviour including obsessive thoughts, repetitive behaviour
- dry mouth
- blurred vision
- increased or decreased sweating
- diarrhoea, nausea, vomiting, heartburn, stomach discomfort or pain
- excessive saliva
- difficulty in swallowing
- weight gain
- mild fever
- changes in sexual function, including prolonged erection
- painful menstruation
- skin reactions, including rash or itching
- urinary problems, including excessive need to urinate, difficulty urinating, dark urine, bedwetting
- joint or muscle pain or muscle weakness

If any of the following happen, tell your doctor immediately or go to your nearest Accident & Emergency department or clinic:

Very common (affects more than 1 in 10 people):
• If you have severe constipation. Your doctor will have to treat this in order to avoid further complications.

Common (affects up to 1 in 10 people):
• if you get signs of a cold, fever, flu-like symptoms, sore throat or any other infection. You will have to have an urgent blood test to check if your symptoms are related to your CLOPINE.
• if you experience seizures (fits).

Uncommon (affects up to 1 in 100 people):
• if you have a sudden rapid increase in body temperature, rigid muscles which may lead to unconsciousness (neuroleptic malignant syndrome) as you may be experiencing a serious side effect which requires immediate treatment.

Rare (affects up to 1 in 1,000 people):
• if you get signs of a respiratory tract infection or pneumonia such as fever, coughing, difficulty breathing, wheezing.
• if you experience nausea (feeling sick), vomiting (being sick) and/or loss of appetite. Your doctor will need to check your liver.
• if you have 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.

Very rare (affects up to 1 in 10,000 people):
• if you are a man and experience persistent painful erection of the penis. This is called priapism. If you have an erection which lasts more than 4 hours immediate medical treatment may be needed in order to avoid further complications
• if you get signs of blood clots in the veins especially in the legs (symptoms include swelling, pain and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing.
• if you experience an allergic reaction (swelling mainly of the face, mouth and throat, as well as, the tongue, which may be itchy or painful).

• if you experience severely decreased urine
• if you experience profuse sweating, headache, nausea, vomiting and diarrhoea
• loss of consciousness or fainting
• chest pain
• sore throat, mouth ulcers, fever, any "flu-like" symptoms such as swollen glands or other signs of infection as these symptoms may be an early sign of agranulocytosis. Flu-like symptoms may also be a sign of myocarditis.
• develop a fast or irregular heart beat that is present even when you are resting, accompanied by rapid breathing, shortness of breath, dizziness or light headedness, or chest pain. These symptoms could be signs of myocarditis, an inflammation of the heart muscle, or another heart condition.
• signs of an allergic reaction such as itching, skin rash, hives, swelling of the face, lips or tongue, difficulty in swallowing or breathing
• signs that blood clots may have formed, such as sudden severe headache, sudden loss of coordination, blurred vision, slurred speech, numbness in an arm or leg
• if you have muscle weakness, fever, fast or irregular heart beat and excessive sweating. These are symptoms of a very rare condition called Neuroleptic Malignant Syndrome (NMS) - a reaction to some medicines, which can cause a sudden increase in body temperature.
• seizures or fits
• stomach pain accompanied by nausea and vomiting
• prolonged or severe constipation, with or without bloating or abdominal pain
• signs of loss of blood sugar control such as excessive thirst, passing large amounts of urine, dry mouth and skin
• unusual bruising or bleeding
• slurred speech, severe headache, blurred vision or loss of vision
• jaundice, yellowing of the skin and/or eyes
• urinary problems - difficulty passing urine (water) or blood in the urine; loss of bladder control
• muscle spasms, stiffness, tremors or restlessness
• loss of co-ordination
• if you have uncontrolled movements of the tongue, jaw (such as puffing at the cheeks, chewing movements, puckering of the mouth), face and mouth. These are symptoms of a very rare condition called tardive dyskinesia - a condition more likely to happen during long term treatment, especially in older women.
• persistent painful erection
• abdominal or lower back pain
• confusion/disorientation

These are serious side effects. You may need urgent medical treatment.

Other side effects not listed above may occur in some patients. Tell your doctor or pharmacist if you notice anything else that is making you unwell. Do not be alarmed by this list of possible side effects. You may not experience any of them.

Product description

What it looks like

CLOPINE 25 – 25 mg tablets are small, round, yellow tablets with "25" embossed over a breakline on one face, the other side is plain.

CLOPINE 50 – 50 mg tablets are small, round, yellow tablets with "50" embossed over a breakline on one face, the other side is plain.

CLOPINE 100 – 100 mg tablets are small, round, yellow tablets with "100", embossed over a breakline on one face, the other side is plain.

CLOPINE 200 – 200 mg tablets are oval shaped yellow tablets with "200" embossed on one side and a breakline on the other side.

CLOPINE 50 mg/mL - a free flowing yellow suspension.

Pack Sizes:
Not all pack sizes may be marketed.

CLOPINE tablets come in packs of 50 or 100 tablets.

CLOPINE 50 mg/mL Suspension is available in a bottle containing 100 mL.

Your doctor will determine the quantity provided to you by the pharmacy.
Ingredients

Active ingredient(s)
clozapine

Inactive ingredients
Tablets:
povidone, microcrystalline cellulose, lactose, sodium starch glycollate, magnesium stearate.
Suspension:
glycerol, hydrochloric acid, monobasic sodium phosphate dihydrate, povidone, purified water, sodium hydroxide, sodium methyl hydroxybenzoate, sodium propyl hydroxybenzoate, sorbitol, xanthan gum.

Sponsor details

CLOPINE is supplied in New Zealand by:
Douglas Pharmaceuticals Ltd
P O Box 45 027
Auckland 0651
New Zealand
Phone: (09) 835 0660

Date of preparation

31 October 2018
(based on data sheet dated 29 October 2018)

Dispensing Instructions

1. Shake the bottle until the suspension is thoroughly mixed.

2. Push down and turn the cap to open the bottle.

3. Push the bottle adaptor into the top of the bottle.

4. Fill the oral dispenser (syringe) with air.

5. Insert the oral dispenser into the opening of the bottle adaptor. Expel all the air from the oral dispenser into the bottle.

6. Turn the bottle upside down.

7. Withdraw the prescribed amount of Clopine Oral Suspension.

8. Turn the bottle upright and remove oral dispenser. Expel any large bubbles.

9. Swallow Clopine Oral Suspension directly from the oral dispenser or add the suspension to a glass with 200 ml of water. Stir and drink the entire mixture right away.

10. Wash the oral dispenser in warm soapy water after each use and rinse well with water. Leave to air dry.

11. Close the bottle with cap provided. The bottle adaptor does not need to be removed before closing.