PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S5

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

CLOMENT 25, 25 mg clozapine per tablet

CLOMENT 100, 100 mg clozapine per tablet

Read all of this leaflet carefully before you start taking CLOMENT tablets

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **CLOMENT** tablets have been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

1. WHAT CLOMENT TABLETS CONTAINS

- The active substance is clozapine 25 mg or 100 mg per tablet
- The other ingredients are lactose, magnesium stearate, microcrystalline cellulose, povidone, purified water and sodium starch glycollate.

2. WHAT CLOMENT TABLETS IS USED FOR

CLOMENT tablets belongs to a class of medicines called atypical antipsychotics.

CLOMENT tablets is used for the treatment of

- treatment-resistant schizophrenia;
- recurrent suicidal behaviour in patients with schizophrenia;
- psychotic disorders in Parkinson's disease.

3. BEFORE YOU TAKE CLOMENT TABLETS

Do not take CLOMENT tablets:

- if you are hypersensitive (allergic) to clozapine or any of the other ingredients of **CLOMENT** tablets (see **WHAT CLOMENT TABLETS CONTAINS**).

- if you are not able to undergo regular blood test.
- if you have a history of granulocytopenia, agranulocytosis or neutropenia (disorders of your white blood cell count or differential blood count).
- if you are taking any medicine that can suppress bone marrow function.
- if you have impaired bone marrow function.
- if you have uncontrolled epilepsy.
- if you are taking medicines containing carbamazepine.
- if you have alcoholic or toxic psychoses, drug intoxication or are in a comatose condition.
- if you have glaucoma.
- if you have circulatory collapse and/or nervous system depression of any cause.
- if you have severe renal or cardiac disorders.
- if you have active liver disease, progressive liver disease or hepatic failure.
- if you have a paralytic ileus.
- if you are younger than 16 years of age.
- if you are immobilized for extended periods of time.

Take special care with CLOMENT tablets:

- if you develop flu-like symptoms (such as fever or sore throat) or any other kind of infection, as it might be an indication that your white blood cell count is dropping. If this happens, you must contact your doctor immediately.
- if you feel dizzy or even faint after standing up or standing for long periods, as **CLOMENT** can cause orthostatic hypotension which is a drop in blood pressure when standing up. If this happens, you must contact your doctor immediately.
- if you have a history of seizures, as **CLOMENT** tablets might cause a seizure attack.
- if you have diabetes or have risk factors for diabetes (e.g. obesity, family history of diabetes), as **CLOMENT** tablets might worsen your glucose control. You should also tell your doctor if you develop symptoms of diabetes or high blood sugar (e.g. increased thirst, urination of a large volume of urine with an increase in urinary frequency, increased appetite and general weakness).

- if you are an elderly patient as you might be more susceptible to the side-effects caused by **CLOMENT** tablets. Your doctor will start your treatment at a low dose and then gradually increase your dose.
- if you are taking any other medicines, as **CLOMENT** tablets has interactions with a wide variety of medicines. Please tell your doctor about any other medicines you are taking before you start taking **CLOMENT** tablets (see **Taking other medicines with CLOMENT tablets**).
- if you stop taking **CLOMENT** tablets for more than two days, you should not start to take it again at the same dosage and should contact your doctor for dosage instructions.
- if you develop symptoms like nausea, vomiting and/or anorexia, you should contact your doctor as it might be an indication of liver dysfunction.
- if you are a smoker and want to quit smoking, as the sudden cessation of smoking might increase the amount of clozapine in your blood.

Before you start taking **CLOMENT** tablets and during your treatment with **CLOMENT** tablets, your doctor will do regular blood tests to monitor your white blood cell count. If your white blood cell count drops below a certain level, your doctor might instruct you to stop taking **CLOMENT** tablets.

Taking CLOMENT tablets with food and drink:

The rate or extent of absorption of **CLOMENT** tablets is not influenced by food.

You must not drink any products containing alcohol while being treated with **CLOMENT** tablets. Some medicines also contains alcohol, so always read the label or ask your doctor or pharmacist if you are unsure.

Products containing caffeine (e.g. coffee) should not be consumed while being treated with **CLOMENT** tablets.

Pregnancy and Breastfeeding

The safe use of **CLOMENT** tablets in pregnant women has not been established. Adequate contraceptive measures must be ensured in women of childbearing potential.

It is not advisable to breastfeed your baby while taking **CLOMENT** tablets.

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other health care professional for advice before taking this medicine.

Driving and using machinery:

Do not drive or operate any tools or machines (especially during the initial weeks of treatment) because **CLOMENT** tablets may make you sleepy and/or dizzy and have the potential to cause seizures.

Taking other medicines with CLOMENT tablets:

Always tell your healthcare professional if you are taking any other medicine.

(This includes complementary or traditional medicines)

CLOMENT tablets might have interactions with the following agents:

- Medicines known to suppress bone marrow function, as **CLOMENT** tablets is known to influence white blood cell counts.
- Anticonvulsant medicines (like valproic acid), as **CLOMENT** tablets can cause seizures while taking valoproic acid.
- Medicines working on the central nervous system like mono-amine oxidase inhibitors, narcotics, antihistamines, benzodiazepines and lithuim as it may enhance the central nervous system depressant effects of **CLOMENT** tablets or increase the risk of developing neuroleptic malignant syndrome.
- Long-acting depot antipsychotics, as they cannot be withdrawn rapidly should there be a drop in white blood cell count.
- Medicines with anticholinergic, hypotensive or respiratory depressant effects, as it may enhance the side-effects of **CLOMENT** tablets.
- Medicines that is highly bound to protein (e.g. warfarin), as clozapine and other highly protein-bound medicines may displace each other from their protein binding sites, possibly resulting in side-effects.
- Selective serotonin re-uptake inhibitors (medicines used to treat depression) such as citalopram, paroxetine, sertraline or fluoxetine, as it may result in elevated concentrations of clozapine (sometimes massive) in your blood.

- Smoking and products containing caffeine and alcohol might influence the concentration of clozapine in your blood (see **Take special care with CLOMENT tablets** and **Taking CLOMENT tablets with food and drink**).

Since the metabolism of clozapine is mediated by an enzyme called cytochrome P450, the concomitant administration of medicines which possess affinity for this enzyme may influence the plasma levels of clozapine and/or the co-administered medicine. Speak to your doctor or pharmacist for further advice.

4. HOW TO TAKE CLOMENT TABLETS

Do not share medicines prescribed for you with any other person.

Always take **CLOMENT** tablets exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The dosage of **CLOMENT** tablets will be adjusted specifically for you, using the lowest possible effective dose. Your treatment will start with one-half of a 25 mg tablet (12,5 mg) and the dose will be gradually increased by your doctor until the desired effect is achieved. **CLOMENT** tablets must be swallowed with a sufficient quantity of water (e.g. half a glass of water). Your total daily dose can be divided unevenly, with the larger portion to be taken at bedtime. If your total daily dose is not more than 200 mg, you can take it as a single dose at bedtime.

Your doctor will tell you how long your treatment with **CLOMENT** tablets will last.

He will also do regular blood tests to monitor your white blood cell count. If your white blood cell count drops too low, your doctor might decide to stop your treatment with **CLOMENT** tablets.

If you have the impression that the effect of **CLOMENT** tablets is too strong or too weak, tell your doctor or pharmacist.

If you take more CLOMENT tablets than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control center.

Signs and symptoms of overdosage: Drowsiness, coma, confusion, hallucinations, agitation, convulsions, increased salivary flow, blurred vision, rapid heartbeat, irregular heartbeat, low blood pressure, difficulty in breathing and collapse.

Treatment of overdosage: Within six hours of ingestion of **CLOMENT** tablets, the stomach should be emptied and activated charcoal administered. Dialysis is unlikely to be effective. Symptomatic treatment is further indicated. Close medical supervision is necessary for several days because of the possibility of delayed reactions.

If you forget to take CLOMENT tablets:

If you forget to take a dose, do not take a double or larger dose to make up for the forgotten individual doses. Continue to take the next dose at the usual time.

If you stop taking **CLOMENT** tablets for more than two days, you should not start to take it again at the same dosage and should contact your doctor for dosage instructions.

Effects when treatment with CLOMENT tablets is stopped:

In the event of planned termination of **CLOMENT** tablets, a gradual reduction in dose is recommended over a 1-2 week period. If immediate discontinuation is necessary, your doctor will observe you carefully for recurrence of psychotic symptoms and symptoms such as profuse sweating, headache, nausea, vomiting and diarrhoea.

5. POSSIBLE SIDE-EFFECTS

CLOMENT tablets can have side-effects. Not all side-effects reported for **CLOMENT** tablets are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **CLOMENT** tablets, please consult your doctor, pharmacist or other health care professional for advice.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Very common

- changes in the way your heart beats, for example, if you notice it beating faster;
- dizziness.

Common

- seizures or convulsions;
- signs of infection such as fever or sore throat;
- fainting or loss of consciousness;
- muscle rigidity and/or tremor (might be an indication of neuroleptic malignant syndrome).

Uncommon

- neuroleptic malignant syndrome.

Rare

- aspiration of ingested food;
- development of blood clots, usually indicated by pain and swelling in the area where the blood clot is.
- hepatitis, jaundice or pancreatitis.

Very rare

- difficulty in breathing;
- intestinal obstruction;
- fulminant hepatic necrosis.

These are all very serious side effects. You may need urgent medical attention.

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

Common

- orthostatic hypotension (a drop in blood pressure upon standing or after standing motionless for a while). Orthostatic hypotension does occur mostly at the beginning of treatment;
- high blood pressure;
- nausea and vomiting.

Rare

- symptoms of high blood sugar concentrations such as increased thirst, urination of a large volume of urine with an increase in urinary frequency, increased appetite and general weakness.

These are all serious side effects. You may need medical attention.

Other side-effects that you might experience:

Very common:

- sedation;
- constipation;
- increased salivary flow.

Common:

- weight gain;
- blurred vision;
- headache;
- abnormal, involuntary movements of your limbs or muscles;
- dry mouth;
- urinary incontinence or urinary retention;
- fatigue;
- disturbances in sweating or temperature regulation.

Rare:

- anaemia;
- restlessness;
- agitation;
- confusion;
- difficulty in swallowing;
- increase in creatinine phosphokinase values.

Very rare:

- ketoacidosis;
- high cholesterol and triglyceride levels;
- skin reactions;
- interstitial nephritis;
- priapism;
- parotid gland enlargement.

If you notice any side-effect not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF CLOMENT TABLETS

Store all medicines out of the reach of children.

Store at or below 25 °C. Protect from light and moisture. Do not refrigerate.

In order to protect from light and moisture, keep the blister strips in the outer carton until ready for use. Keep the outer carton tightly closed. Do not store **CLOMENT** tablets in areas of high humidity or temperature (e.g. bathrooms and kitchens).

Do not use after the expiry date stated on the outer carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF CLOMENT TABLETS

CLOMENT 25: Clear transparent blister packs of 100 tablets packed in an outer carton.

CLOMENT 100: Clear transparent blister packs of 100 tablets packed in an outer carton.

8. IDENTIFICATION OF CLOMENT TABLETS

CLOMENT 25: A round, yellow flat bevel-edged tablet with '25' over a pressure sensitive breakline on one side, and plain on the other side.

CLOMENT 100: A round, yellow flat bevel-edged tablet with '100' over a pressure sensitive breakline on one side, and plain on the other side.

9. REGISTRATION NUMBERS

CLOMENT 25: 35/2.6.5/0373

CLOMENT 100: 35/2.6.5/0374

10. NAME AND ADDRESS OF REGISTRATION HOLDER

Acino Pharma (Pty) Ltd

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MIDRAND

11. DATE OF PUBLICATION

8 August 2002