

ANZARIL TABLET

Clozapine (25mg, 100mg)

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What Anzaril Tablet is used for

Clozapine is the active ingredient of Anzaril Tablet. It is indicated in people with treatment-resistant schizophrenic only i.e schizophrenic (a severe brain disorder in which people interpret reality abnormally) people who are non-responsive to or intolerant to classic neuroleptic (antipsychotic) medicines.

How Anzaril Tablet works

Clozapine is a psychiatric medication (antipsychotic type) that works by changing the activity of certain natural substances in the brain.

Before you use Anzaril Tablet

- When you must not use it

- If you are allergic (hypersensitive) or to clozapine or any other components of the formulations.
- If you have a history of toxic or idiosyncratic granulocytopenia/agranulocytosis (low white blood cell count).
- If you have impaired bone marrow function.
- If you have uncontrolled epilepsy.
- If you have alcoholic and other toxic mental disorder, drug intoxication and comatose conditions.
- If you have circulatory collapse (rapid or sudden development of circulatory failure) and/or CNS depression (physiological

depression of the central nervous system that can result in decreased rate of breathing, decreased heart rate, and loss of consciousness possibly leading to coma or death) of any cause.

- If you have severe kidney or heart disorders.
- If you have active liver disease associated with nausea, anorexia (eating disorder), jaundice, progressive liver disease or liver failure.

- Before you start to use it

You must tell your doctor if:

- You have allergies to any medicine which you have taken previously to treat your current condition.
- You are pregnant, trying to become pregnant or breast-feeding.
- You are taking medicine known to have a substantial potential to depress bone marrow function.
- You are suffering from high blood glucose level or diabetes mellitus.
- You are have prostate enlargement (an increase in the size of the prostate gland causing difficulty urinating) and narrow-angle glaucoma (increased pressure in the eye).

Safety and effectiveness of its use in children have not been established.

- Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any of these medicines:

- Alcohol, monoamine oxidase inhibitors (MAOIs) inhibitors and central nervous system (CNS) depressants such as antihistamine – may enhance the central effect.
- Benzodiazepine and other psychotropic medicines – increased risk of circulatory

collapse which may lead to cardiac arrest (sudden cessation of heartbeat and heart function, resulting in the loss of effective circulation) and/or respiratory arrest (cessation of breathing).

- Medicines possessing anticholinergic, blood pressure lowering or respiratory depressant effects – possibility of additive effects
- Lithium or central nervous system (CNS) active agents – increase risk of development of neuroleptic malignant syndrome (NMS). NMS is a life-threatening neurological disorder most often caused by an adverse reaction to neuroleptic or antipsychotic medicines.
- Norepinephrine – may reduce the blood pressure increasing effect of Norepinephrine.
- Valproic acid – onset of seizures in non-epileptic individuals and isolated cases of delirium (a serious disturbance in mental abilities that results in confused thinking and reduced awareness of your environment).
- Carbamazepine, phenytoin and rifampicin, omeprazole, nicotine – decrease the blood levels of clozapine.
- Cimetidine, erythromycin and fluvoxamine,azole antimycotics, protease inhibitors, caffeine, paroxetine, sertraline, fluoxetine – increase blood levels of clozapine.

Always inform your doctor and pharmacist if you are taking any other medicines, including herbal tonics, supplements and medicines that you buy without prescription.

Talk to your pharmacist or doctor if you are not sure about this.

How to use Anzaril Tablet

Always take this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. Take this medicine only by mouth.

- How much to use

Starting therapy

12.5mg once or twice on the 1st day, followed by one or two 25mg tablets on the 2nd day. If well tolerated, daily dose may be increase slowly in increments of 25mg to 50mg in order to achieve a dose level of up to 300mg/day within 2-3 weeks. Thereafter, if required, the daily dose may be further increased in increments of 50mg to 100mg at half-weekly or preferably weekly intervals.

Use in elderly

Initiate treatment at 12.5mg given once and restrict subsequent dose increments to 25mg/day.

Therapeutic dose

300-450mg per day in divided dose. Some may require up to 600mg per day.

Maximum Dose

900mg per day.

Maintenance Dose

The possibility of increase in adverse reactions (in particular seizures) occurring at doses over 450mg/ day must be borne in mind.

Ending Dose

Gradual reduction over 1-2 week period is recommended.

Restarting Therapy

In individual whom the interval since the last dose exceeds 2 days, treatment should be re-initiated at 12.5mg given once or twice on the 1st day.

Switching from previous neuroleptic therapy to Clozapine.

It is recommended that the other neuroleptics should be discontinued by tapering the dosage downwards over a period of approximately 1 week. Once the neuroleptic has been completely discontinued over 24 hours, clozapine treatment can be started as described above.

- When to use it

The total daily dose may be divided unevenly, with the larger portion at bedtime. If the daily dose does not exceed 200mg, once daily administration in the evening may be appropriate.

- How long to use it

Continue taking Anzaril Tablet for as long as your doctor recommends.

- If you forget to use it

- If you forget a dose, take it as soon as you remember it.
- However, if it is nearly time for the next dose, skip the missed dose.
- Do not take a double dose to make up for a forgotten dose.

- If you use too much (overdose)

Symptoms: lethargy (tiredness), drowsiness, areflexia (absence of reflexes) , coma, confusion, hallucinations (hearing voices or seeing things which are not there) , agitation, delirium (confused thinking and reduced alertness), extrapyramidal symptoms (physical symptoms including tremor, slurred speech, anxiety, distress and paranoia), hyper-reflexia (overactive or overresponsive reflexes), convulsions, hypersalivation (excessive production of saliva), mydriasis (great dilatation of the pupil), blurred vision, thermolability , low blood pressure, collapse, rapid heart beat, cardiac arrhythmias (irregular heartbeat), aspiration pneumonia (inflammatory of the lungs and large airway), dyspnoea (shortness of breath), respiratory depression or failure.

Close medication supervision is necessary for at least 5 days because of the possibility of delayed reactions.

Contact your doctor immediately or go to the Emergency Department of your nearest hospital, if you think you or anyone else may have taken too much of this medicine. Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention.

While you are using it

- Things you must do

- Contact your doctor if your symptoms worsen or they do not improve.
- Your doctor will check and monitor your white blood count and absolute neutrophil count prior to treatment and weekly for 18 weeks then monthly thereafter.
- Contact your doctor if any kind of infection, fever, sore throat or other flu-like symptoms develop.
- Contact your doctor immediately if you suffers from tachycardia (abnormal rapid heart rate) that persists at rest, accompanied by arrhythmias (an irregular or abnormal rhythm of heart beat), shortness of breath or signs and symptoms of heart failure.
- You must be monitored for worsening of glucose control if you are suffering from diabetes mellitus.
- You must discontinue the treatment if you develop jaundice.

- Things you must not do

Do not give Anzaril Tablet to anyone else, even if their symptoms seem similar or they have same condition as you. Your doctor has prescribed Anzaril Tablet for you and your condition.

- **Thing to be careful of**
This medicine will affect your ability to drive or use machines. If the tablets make you feel sick, dizzy or tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

Side effects

Like all medicines, Anzaril Tablet can have side effects, although not everybody gets them. The following side effects may happen with this medicine.

- Haematological – development of granulocytopenia and agranulocytosis (an abnormally low number of granular white blood cells in the blood). Unexplained leucocytosis (an increase in the number of white cells in the blood) and / or eosinophilia (an increase in the number of eosinophils in the blood) may occur especially in the initial weeks of treatment. Very rarely, thrombocytopenia (deficiency of platelets in the blood).
- Central nervous system – fatigue, drowsiness and sedation. Dizziness or headache may also occur. Very rarely, clozapine may cause confusion, restlessness, agitation and delirium. Extrapyramidal effects may also occur.
- Autonomic nervous system – dry mouth, blurred vision, disturbances in sweating and temperature regulation.
- Cardiovascular system – rapid heart beat and postural low blood pressure. Less commonly high blood pressure.
- Respiratory system – respiratory depression or arrest has occurred.
- Gastrointestinal system – nausea, vomiting, constipation and very rarely, intestinal obstruction.
- Genitourinary system – urinary incontinence (involuntary loss of urine from the bladder) and urinary retention. Priapism (prolonged erection of the penis) has been reported.
- Miscellaneous – benign hyperthermia (body temperature rises to levels higher than normal), isolated report of skin reactions,

severe hyperglycemia (high blood sugar), increase in creatine phosphokinase (CPK) value, considerable weight gain, sudden and unexplained deaths.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Consult your doctor or pharmacist if you are in doubt or for any further information.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website portal.bpfk.gov.my (Consumers→Reporting)

Storage and Disposal of Anzaril Tablet

- **Storage**
Do not use after the expiry date stated on the pack. The expiry date refers to the last day of that month.

Store below 30°C in well closed container. Protect from light, heat and moisture.

Keep out of the reach and sight of children.

- **Disposal**
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required.

These measures will help to protect the environment.

Product Description

Anzaril 25mg tablet

- **What it looks like**
A yellow, scored, flat of diameter 7mm round tablet with 'MPI' marked.

They are supplied in 10x10's blisterpack.

- **Ingredients**

- Active ingredient
Each tablet contains 25mg of the active substance, Clozapine.
- Inactive ingredients
The other ingredients are lactose, corn starch, sodium lauryl sulphate, povidone k-30, magnesium stearate and colloidal silicone dioxide.

Anzaril 100mg tablet

- **What it looks like**
A yellow, flat-bevelled edge tablet with scored at one side, marked 'MPI' on the other, diameter of 10mm round tablet.

They are supplied in 10x10's blisterpack.

- **Ingredients**

- Active ingredient
Each tablet contains 100mg of the active substance, Clozapine.
- Inactive ingredients
The other ingredients are lactose, corn starch, sodium lauryl sulphate, povidone k-30, magnesium stearate and colloidal silicone dioxide.

- **MAL number:**
Anzaril Tablet 25mg
MAL06100580AZ

Anzaril Tablet 100mg
MAL06100579AZ

Manufacturer and Product Registration Holder

Malaysian Pharmaceutical Industries Sdn. Bhd.
Plot 14, Lebuhraya Kampung Jawa, 11900 Bayan Lepas, Penang, Malaysia.

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