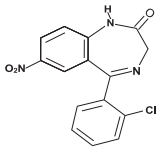
# Magura® 0.5mg / 2mg Tablets
(Clonazepam)

**DESCRIPTION:**
**Magura®** contains clonazepam, a benzodiazepine, available in 0.5mg and 2mg tablets

**COMPOSITION:**
**Magura® 0.5mg Tablets**
Each tablet contains:
Clonazepam USP .....0.5mg

**Magura® 2mg Tablets**
Each tablet contains:
Clonazepam USP .....2mg




**CLINICAL PHARMACOLOGY:**
The precise mechanism by which clonazepam exerts its antiseizure and antipanic effects is unknown, although it is believed to be related to its ability to enhance the activity of gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the central nervous system. Convulsions produced in rodents by pentylenetetrazol or, to a lesser extent, electrical stimulation are antagonized, as are convulsions produced by photic stimulation in susceptible baboons. A taming effect in aggressive primates, muscle weakness and hypnosis are also produced. In humans, clonazepam is capable of suppressing the spike and wave discharge in absence seizures (Petit mal) and decreasing the frequency, amplitude, duration and spread of discharge in minor motor seizures

**PHARMACOKINETICS:**
Clonazepam is rapidly and completely absorbed after oral administration. The absolute bioavailability of clonazepam is about 90%. Maximum plasma concentration of clonazepam is reached within 1 to 4 hours after oral administration. Clonazepam is approximately 85% bound to plasma proteins. Clonazepam is highly metabolized, with less than 2% unchanged clonazepam being excreted in the urine. Biotransformation occurs mainly by reduction of the 7-nitro group to the 4-amino derivative. This derivative can be acetylated, hydroxylated and glucuronidated. Cytochrome P-450 including CYP3A, may play an important role in clonazepam reduction and oxidation. The elimination half-life of clonazepam is typically 30 to 40 hours. Clonazepam pharmacokinetic is dose-independent throughout the dosing range

**INDICATIONS AND USAGE:**
**Seizure Disorders:** Clonazepam is useful alone or as an adjunct in the treatment of the Lennox-Gastaut syndrome (Petit mal variant), akinetic and myoclonic seizures. In patients with absence seizures (Petit mal) who have failed to respond to succinimides, clonazepam may be useful

**Panic Disorder:** Clonazepam is indicated for the treatment of panic disorder, with or without agoraphobia, as defined in DSM-IV

**CONTRAINDICATIONS:**
Clonazepam should not be used in patients with a history of sensitivity to benzodiazepines, or in patients with clinical or biochemical evidence of significant liver disease. It may be used in patients with open angle glaucoma who are receiving appropriate therapy but is contraindicated in acute narrow angle glaucoma

**WARNINGS:**
**Interference with Cognitive and Motor Performance:** Since clonazepam produces CNS depression, patients receiving this drug should be cautioned against engaging in hazardous occupations requiring mental alertness, such as operating machinery or driving a motor vehicle

**Suicidal Behavior and Ideation:** Antiepileptic drugs (AEDs) including clonazepam, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior

**Withdrawal Symptoms:** Withdrawal symptoms of the barbiturate type have occurred after the discontinuation of benzodiazepines

**PRECAUTIONS:**
**General: Worsening of Seizures:** When used in patients in whom several different types of seizure disorders coexist, clonazepam may increase the incidence or precipitate the onset of generalized tonic-clonic seizures (Grand mal). This may require the addition of appropriate anticonvulsants or an increase in their dosages. The concomitant use of valproic acid and clonazepam may produce absence status

**Risks of Abrupt Withdrawal:** The abrupt withdrawal of clonazepam, particularly in those patients on long-term, high-dose therapy, may precipitate status epilepticus. Therefore, when discontinuing clonazepam, gradual withdrawal is essential. While clonazepam is being gradually withdrawn, the simultaneous substitution of another anticonvulsant may be indicated

**Caution in Renally Impaired Patients:** Metabolites of clonazepam are excreted by the kidneys; to avoid their excess accumulation, caution should be exercised in the administration of the drug to patients with impaired renal function

**Hypersalivation:** Clonazepam may produce an increase in salivation. This should be considered before giving the drug to patients who have difficulty handling secretions. Because of this and the possibility of respiratory depression, clonazepam should be used with caution in patients with chronic respiratory diseases

**Drug Interactions:** The CNS-depressant action of the benzodiazepine class of drugs may be potentiated by alcohol, narcotics, barbiturates, nonbarbiturate hypnotics, antianxiety agents, the phenothiazine, thioxanthene and butyrophenone classes of antipsychotic agents, monoamine oxidase inhibitors and the tricyclic antidepressants, and by other anticonvulsant drugs

**Pregnancy: Teratogenic Effects:** Pregnancy Category D

**Nursing Mothers:** Mothers receiving clonazepam should not breastfeed their infants

**Paediatric Use:** Because of the possibility that adverse effects on physical or mental development could become apparent only after many years, a benefit-risk consideration of the long-term use of clonazepam is important in paediatric patients being treated for seizure disorder. Safety and effectiveness in paediatric patients with panic disorder below the age of 18 have not been established

210mm

150mm

**ADVERSE REACTIONS:**
**Seizure Disorders:** The most frequently occurring side effects of clonazepam are CNS depression. Drowsiness, ataxia and behavior problems have been noted
**Neurologic:** Abnormal eye movements, aphonia, choreiform movements, coma, diplopia, dysarthria, dysdiadochokinesis, "glassy-eyed" appearance, headache, hemiparesis, hypotonia, nystagmus, respiratory depression, slurred speech, tremor and vertigo
**Psychiatric:** Confusion, depression, amnesia, hallucinations, hysteria, increased libido, insomnia and psychosis
**Paradoxical reactions:** Excitability, irritability, aggressive behavior, agitation, nervousness, hostility, anxiety, sleep disturbances, nightmares and vivid dreams
**Respiratory:** Chest congestion, rhinorrhoea, shortness of breath, hypersecretion in upper respiratory passages
**Cardiovascular:** Palpitation
**Dermatologic:** Hair loss, hirsutism, skin rash, ankle and facial edema
**Gastrointestinal:** Anorexia, coated tongue, constipation, diarrhoea, dry mouth, encopresis, gastritis, increased appetite, nausea and sore gums
**Genitourinary:** Dysuria, enuresis, nocturia and urinary retention
**Musculoskeletal:** Muscle weakness and pain
**Hepatic:** Hepatomegaly, transient elevations of serum transaminases and alkaline phosphatase
**Hematopoietic**: Anemia, leukopenia, thrombocytopenia, eosinophilia
**Miscellaneous:** Dehydration, general deterioration, fever, lymphadenopathy, weight loss or gain

**OVERDOSAGE:**
Symptoms of clonazepam overdosage, like those produced by other CNS depressants include somnolence, confusion, coma and diminished reflexes

**DOSAGE AND ADMINISTRATION:**
**Seizure Disorders**
**Adults:** The initial dose for adults with seizure disorders should not exceed 1.5mg/day divided into three doses. Dosage may be increased in increments of 0.5 to 1mg every 3 days until seizures are adequately controlled or until side effects preclude any further increase. Maintenance dosage must be individualized for each patient depending upon response. Maximum recommended daily dose is 20mg
The use of multiple anticonvulsants may result in an increase of depressant adverse effects. This should be considered before adding clonazepam to an existing anticonvulsant regimen
**Paediatric Patients**: Clonazepam is administered orally. In order to minimize drowsiness, the initial dose for infants and children (Up to 10 years of age or 30kg of body weight) should be between 0.01 and 0.03mg/kg/day but not to exceed 0.05mg/kg/day given in two or three divided doses. Dosage should be increased by not more than 0.25 to 0.5mg every third day until a daily maintenance dose of 0.1 to 0.2mg/kg of body weight has been reached, unless seizures are controlled or side effects preclude further increase. Whenever possible, the daily dose should be divided into three equal doses. If doses are not equally divided, the largest dose should be given before retiring
**Geriatric Patients**: There is no clinical trial experience with clonazepam in seizure disorder patients 65 years of age and older. In general, elderly patients should be started on low doses of clonazepam and observed closely

**Panic Disorder**
**Adults:** The initial dose for adults with panic disorder is 0.25mg b.i.d. An increase to the target dose for most patients of 1mg/day may be made after 3 days. The recommended dose of 1mg/day is based on the results from a fixed dose study in which the optimal effect was seen at 1mg/day. Higher doses of 2, 3 and 4mg/day in that study were less effective than the 1mg/day dose and were associated with more adverse effects. Nevertheless, it is possible that some individual patients may benefit from doses of up to a maximum dose of 4mg/day, and in those instances, the dose may be increased in increments of 0.125 to 0.25mg b.i.d. every 3 days until panic disorder is controlled or until side effects make further increases undesired. To reduce the inconvenience of somnolence, administration of one dose at bedtime may be desirable
Treatment should be discontinued gradually, with a decrease of 0.125mg b.i.d. every 3 days, until the drug is completely withdrawn
There is no body of evidence available to answer the question of how long the patient treated with clonazepam should remain on it. Therefore, the physician who elects to use clonazepam for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient
**Paediatric Patients:** There is no clinical trial experience with clonazepam in panic disorder patients under 18 years of age
**Geriatric Patients:** There is no clinical trial experience with clonazepam in panic disorder patients 65 years of age and older. In general, elderly patients should be started on low doses of clonazepam and observed closely

**OR**
As directed by the physician

**STABILITY:**
See expiry on the pack

**PRESENTATION:**
**Magura®** 0.5mg tablets in a pack of 50's
**Magura®** 2mg tablets in a pack of 30's

**INSTRUCTIONS:**
Keep out of the reach of children
Avoid exposure to heat, light and humidity
Store between 15 to 30°C
Improper storage may deteriorate the medicine

میگورا ۰٫۵ ملی گرام / ۲ ملی گرام ٹیبلٹ
(کلونازیپام)

**خوراک:** ڈاکٹر کی ہدایت کے مطابق استعمال کریں
بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ
کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

Manufactured by:
**SAMI Pharmaceuticals (Pvt.) Ltd.**
F-95, S.I.T.E., Karachi-Pakistan
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R.N-03/HA/05/16/Pampac

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