

# SEREPAM

Tablets

## Composition

### Serepam 5 mg Tablets

Each tablet contains Diazepam 5 mg.

## Action

Diazepam is a benzodiazepine tranquillizer that is believed to act by facilitating the synaptic actions of gamma aminobutyric acid (GABA). GABA is one of the major inhibitory neurotransmitters of the CNS. Diazepam does not act at the same site as GABA, but at a presumably allosterically linked site, called the benzodiazepine receptor. It is through this site that the anticonvulsant, sedative, skeletal muscle relaxant, and amnesic properties of diazepam are mediated.

## Pharmacokinetics

Diazepam is readily and completely absorbed from the gastrointestinal tract. Peak plasma concentrations occur in 30-90 minutes after administration, but may be further delayed in elderly patients. Diazepam has a biphasic elimination curve, the terminal half-life being 1-2 days. It is extensively protein-bound.

Diazepam is metabolised in the liver and the following active metabolites are produced: desmethyldiazepam, methyloxazepam, oxazepam, and temazepam. The metabolites are then eliminated by the kidneys in either their free or conjugated form. The half-life of diazepam is prolonged in patients with kidney or liver disease. Diazepam and its active metabolites show significant accumulation during multiple dosage regimens. Steady state plasma concentrations are attained in 5 days to 2 weeks, as some of its metabolites take several days to weeks to be eliminated.

## Indications

### Anxiety

For the management of anxiety disorders or for the short-term relief of the symptoms of anxiety.

### Acute Alcohol Withdrawal

May be useful in symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis.

### Muscle Relaxant

As an adjunct for the treatment of skeletal muscle spasm due to reflex spasm of local pathology (e.g. inflammation of muscles or joints or secondary trauma), spasticity caused by upper motor neuron disorders (e.g. cerebral palsy and paraplegia), athetosis, stiff-man syndrome.

### Anticonvulsant

Oral diazepam may be used adjunctively in convulsive disorders, although it has not proved useful as the sole therapeutic agent.

## Contraindications

- Known hypersensitivity to benzodiazepines.
- Acute pulmonary insufficiency, psychoses.
- First trimester of pregnancy and in breastfeeding.
- Acute narrow-angle glaucoma (benzodiazepines may be used in patients with open-angle glaucoma who are receiving appropriate therapy).

## Warnings

Prolonged use may cause dependence.

Withdrawal symptoms similar in character to those noted with barbiturates and alcohol have occurred following abrupt discontinuation of benzodiazepine drugs. These symptoms include convulsions, tremor, abdominal and muscle cramps, vomiting and sweating.

When discontinuing therapy in patients who have used these agents for prolonged periods, the dosage should be decreased gradually to avoid the possibility of withdrawal symptoms. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, rage, insomnia, sleep disturbances and stimulation have been reported. Should these occur, use of the drug should be discontinued.

### **Pregnancy**

#### *Category C*

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

### **Nursing Mothers**

Benzodiazepines are excreted in breast milk. Since neonates metabolize this drug more slowly than adults, and accumulation of the drug and its metabolites to toxic levels is possible, it should not be administered to nursing women .

### **Adverse Reactions**

Adverse Reactions with different benzodiazepines vary in type and frequency. Some are dose-related, while others involve individual patient sensitivity. Although not all of the following adverse reactions have been attributed specifically to each benzodiazepine drug, the potential for their occurrence exists. This should be borne in mind when drugs of this class are administered.

The most-commonly reported side effects have been drowsiness, fatigue and ataxia, especially in elderly or debilitated patients. Infrequently reported side effects are listed below.

#### **Central Nervous System**

Sedation and sleepiness, depression, lethargy, apathy, hypoactivity, light-headedness, disorientation, restlessness, confusion, delirium, headache, slurred speech, dysarthria, syncope, vertigo, dizziness, nervousness, vivid dreams, psychomotor retardation.

#### **Gastrointestinal**

Constipation, diarrhea, dry mouth, nausea, vomiting and increased salivation.

#### **Genitourinary**

Incontinence, dysuria, enuresis, changes in libido, urinary retention and menstrual irregularities.

#### **Cardiovascular**

Bradycardia, tachycardia, hypertension, hypotension and palpitations.

#### **Ophthalmological**

Visual disturbances, diplopia.

#### **Dermatological**

Urticaria, pruritus, skin rash and dermatitis.

#### **Other**

Hepatic dysfunction (including hepatitis and jaundice), blood dyscrasias including agranulocytosis, anemia, thrombocytopenia and eosinophilia.

### **Precautions**

In elderly or debilitated patients and in children, the initial dose should be low. Dosage increments should be made gradually, according to the response of the patient, in order to preclude ataxia or excessive sedation.

Although hypotension has rarely occurred, the drug should be administered with caution to patients in whom a drop in blood pressure might lead to cardiac complications. Caution should be exercised in patients with impaired renal or hepatic function, and in patients with chronic pulmonary insufficiency.

Patients who experience drowsiness during treatment should be warned that their ability to perform potentially hazardous tasks requiring mental alertness or physical coordination, such as driving a vehicle or operating machinery, may be impaired. Similarly, children should be warned not to participate in activities such as riding a bicycle or playing near traffic. Because of its muscular relaxant effect, particular caution must be exercised when administering the drug to patients with myasthenia gravis.

### **Drug Interactions**

If Diazepam is given concomitantly with centrally acting drugs such as neuroleptics, tranquillizers, antidepressants, hypnotics, analgesics and anaesthetics, the sedative effects are likely to be intensified. The elderly require special supervision.

#### *Diazepam / alcohol or CNS depressants*

The dosage of one or both should be decreased. If diazepam is used with opioid analgesics, the dosage of the opioid analgesic should be decreased by at least one third.

#### *Diazepam / antacids*

Concurrent use of these delays the absorption of diazepam.

#### *Diazepam / tricyclic antidepressants*

Concurrent use of these increases the CNS depressant effects.

#### *Diazepam / carbamazepine*

Concurrent use results in an increase in hepatic metabolism, due to induction of hepatic microsomal enzyme activity leading to decreased serum concentrations and decreased elimination half-lives of diazepam. Monitoring blood concentrations is recommended, especially if carbamazepine is added or withdrawn from existing diazepam therapy.

#### *Diazepam / cimetidine, oestrogen-containing oral contraceptive, disulfiram and erythromycin*

Concurrent use of these inhibits hepatic metabolism (oxidation) of diazepam, therefore delays its elimination, and increases diazepam plasma concentrations.

#### *Diazepam / isoniazid*

Concurrent use may inhibit diazepam elimination.

#### *Diazepam / levodopa*

Concurrent use may decrease the therapeutic effects of levodopa.

#### *Diazepam / rifampin*

Enhances the elimination of diazepam, therefore, decreases plasma concentrations. Dosage adjustment necessary.

#### *Diazepam / zidovudine*

Benzodiazepine competitively inhibits hepatic glucuronidation of zidovudine and therefore decreases its clearance that leads to toxicity. Avoid concurrent use.

### **Dosage and Administration**

Dosage should be individualized for maximum beneficial effect. Average doses are as follows:

#### **Adults**

*Anxiety Disorders and Relief of Symptoms of Anxiety*

5-10 mg, 2-4 times daily, is depending upon severity of symptoms.

*Symptomatic Relief in Acute Alcohol Withdrawal*

10 mg, 3 or 4 times during the first 24 hours, reducing to 5 mg, 3 or 4 times daily, as needed.

*Adjunctively for Relief of Skeletal Muscle Spasm*

5-10 mg, 3 or 4 times daily.

*Adjunctively in Convulsive Disorders*

5-10 mg, 2-4 times daily.

**Geriatric Patients or Patients with Debilitating Disease**

2.5 mg, 1-2 times daily initially, gradually increase, as needed and tolerated.

**Children**

Not for use in children under 6 months.

Because of varied responses to CNS-acting drugs, therapy should be initiated with the lowest dose, and increased as required.

1-2.5 mg, 3 or 4 times daily initially, gradually increase, as needed and tolerated.

**Over Dosage**

**Manifestations**

Somnolence, confusion and coma, reduced or absent reflexes, respiratory depression and hypotension.

**Treatment**

If the patient is conscious, vomiting should be induced either mechanically or with emetics.

If the patient is unconscious, gastric lavage utilizing a cuffed endotracheal tube to prevent aspiration and pulmonary complications should be employed.

General supportive measures should be employed along with intravenous fluids. An adequate airway should be maintained.

Hypotension may be combated by the administration of noradrenaline or metaraminol.

If excitation occurs, barbiturates should not be used.

Dialysis is of limited value.

**Presentation**

**Serepam 5 mg Tablets**

Box of 20 tablets