

This product is no longer marketed in New Zealand and this data sheet may not be up to date. A more up-to-date data sheet for a product with the same active ingredient may be available on the Medsafe website.

# PROPAM

## *Diazepam*

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### Presentation

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*Propam 2 mg Tablets:* White flat bevel edged tablet, 9/32" diameter, imprinted 'DM' with a bisect on one side.

*Propam 5 mg Tablets:* Yellow flat bevel edged tablet, 9/32" diameter, imprinted 'DM' with a bisect on one side.

*Propam 10 mg Tablets:* Blue flat bevel edged tablet, 9/32" diameter, imprinted 'DM' with a bisect on one side.

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### Uses

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#### **Actions**

Diazepam is a benzodiazepine tranquilliser 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**

##### **Adults:**

Short-term (2-4 weeks) symptomatic treatment of anxiety that is severe, disabling or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic or psychotic illness.

Short-term (2-4 weeks) treatment of conditions where anxiety may be a precipitating or aggravating factor, e.g. tension headaches or migraine attacks.

Symptomatic treatment of acute alcohol withdrawal.

Muscle spasm. As an adjunct to the control of muscle spasm in tetanus.

May be useful in the management of cerebral spasticity in selected cases.

As an adjunct to the management of some types of epilepsy, e.g. myoclonus.

Premedication.

**Children:**

Night terrors and somnambulism.

May be useful in controlling tension and irritability in cerebral spasticity in selected cases.

As an adjunct to the control of muscle spasm in tetanus.

Premedication.

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## **Dosage and Administration**

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***Anxiety states:***

**Adults:**

Usual dose: 2 mg three times daily.

Maximum dose: Up to 30 mg daily in divided doses. Adjusted on an individual basis.

Insomnia associated with anxiety: 5 to 15 mg before retiring.

The lowest dose which can control symptoms should be used. Treatment should not be continued at the full dose beyond four weeks. Long-term chronic use is not recommended. Treatment should always be tapered off gradually. Patients who have taken benzodiazepines for a prolonged time may require a longer period during which doses are reduced. Specialist help may be appropriate.

***Symptomatic relief of acute alcohol withdrawal:***

**Adults:**

5 to 20 mg, repeated if necessary in 2 to 4 hours.

***Night terrors and somnambulism:***

**Children:**

1 to 5 mg at bedtime.

***Conditions associated with muscle spasm:***

**Adults:**

Muscle spasm: 2 to 15 mg daily in divided doses.

Management of cerebral spasticity in selected cases: 2 to 60 mg daily in divided doses.

Adjunct to control of muscle spasm in tetanus: 3 to 10 mg/kg body-weight daily by nasoduodenal tube. The selected dose should relate to the severity of the case and in extremely severe cases higher doses have been used.

**Children:**

Control of tension and irritability in cerebral spasticity in selected cases: 2 to 40 mg daily in divided doses.

As an adjunct to the control of muscle spasm in tetanus: As for adults

***Adjunct to the management to some types of epilepsy:***

**Adults:**

2 to 60 mg daily in divided doses

***Premedication:*****Adults:**

5 to 20 mg

**Children:**

2 to 10 mg

**Elderly or debilitated patients:**

Doses should not exceed half those normally recommended.

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## Contraindications

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Diazepam should not be given to patients with acute closed-angle glaucoma, or a predisposition to it, myasthenia gravis, severe chronic obstructive pulmonary disease, hyperkinesia and children with swallowing abnormalities.

Diazepam should also be avoided in psychotic patients with mental illness or suicidal tendencies unless there is a marked component of anxiety.

Also avoid use in patients with hypersensitivity to diazepam.

Diazepam is also contraindicated in acute alcohol intoxication with depressed vital signs and in patients with a history of drug abuse or dependence.

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## Warnings and Precautions

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In patients with chronic pulmonary insufficiency, and in patients with chronic renal or hepatic disease, dosage may need to be reduced.

Amnesia may occur.

In cases of loss or bereavement, psychological adjustment may be inhibited by benzodiazepines.

The dependence potential of the benzodiazepines is low but this increases when high doses are used, especially when given over long periods. This is particularly so in patients with a history of alcoholism or drug abuse or in patients with marked personality disorders. Regular monitoring in such patients is essential, routine repeat prescriptions should be avoided and treatment should be withdrawn gradually. Symptoms such as depression, nervousness, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment in patients receiving even normal therapeutic doses for short periods of time.

In rare instances, withdrawal following excessive dosages may produce confusional states, psychotic manifestations and convulsions.

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural effects include paradoxical aggressive outbursts, excitement, confusion, and the uncovering of depression with suicidal tendencies.

Disinhibiting effects may be manifested in various ways. Suicide may be precipitated in patients who are depressed, and aggressive behaviour towards self and others may be precipitated. Extreme caution should therefore be used in prescribing benzodiazepines to patients with personality disorders.

In patients with myasthenia gravis, who are prescribed diazepam, care should be taken on account of pre-existing muscle weakness.

Withdrawal from benzodiazepines may be associated with physiological and psychological symptoms of withdrawal including depression.

Withdrawal symptoms occur with benzodiazepines following normal therapeutic doses given for short periods of time.

An underlying cause for insomnia should be sought before deciding upon the use of benzodiazepines for symptomatic relief.

This product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

### ***Use in Pregnancy:***

If the product is prescribed to a woman of childbearing potential, she should be warned to contact her physician regarding discontinuance of the product if she intends to become or suspects that she is pregnant.

If for compelling medical reasons, the product is administered during the late phase of pregnancy, or during labour at high doses, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected, due to the pharmacological action of the compound. Moreover, infants born to mothers who took benzodiazepines chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk for developing withdrawal symptoms in the postnatal period.

### ***Use in Lactation:***

Since benzodiazepines are found in breast milk, benzodiazepines should not be given to breast feeding mothers.

### ***Effects on Ability to Drive and Use Machines***

Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or to use machines. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased (see also Interactions).

Patients should be advised that, like all medicaments of this type, diazepam may modify patients' performance at skilled tasks (driving, operating machinery, etc) to a varying degree depending on dosage, administration and individual susceptibility. Patients should further be advised that alcohol may intensify any impairment and should, therefore be avoided during treatment.

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## **Adverse Effects**

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Common adverse effects include drowsiness, sedation, unsteadiness and ataxia. These effects occur following single as well as repeated dosage, and may persist into the following day.

The elderly are particularly sensitive to the effects of centrally-depressant drugs and may experience confusion, especially if organic brain changes are present; the dosage of diazepam should not exceed one half that recommended for other adults.

Other adverse effects are rare and include headache, vertigo, hypotension, gastrointestinal upsets, skin rashes, visual disturbances, changes in libido and urinary retention. Isolated cases of blood dyscrasias and jaundice have also been reported.

Paradoxical reactions such as acute hyperexcitation, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should any of these reactions occur, the use of the drug should be discontinued.

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## Interactions

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### Not recommended:

Concomitant intake with alcohol. The sedative effect may be enhanced when the product is used in combination with alcohol. This affects the ability to drive or use machines.

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

Pharmacokinetic studies on potential interactions between diazepam and anti-epileptic drugs have produced conflicting results. Both depression and elevation of drug levels, as well as no change, have been reported.

When diazepam is used in conjunction with anti-epileptic drugs, side-effects and toxicity may be more evident, particularly with hydantoins or barbiturates or combinations including them. This requires extra care in adjusting dosage in the initial stages of treatment.

Known inhibitors of hepatic enzymes eg. cimetidine and omeprazole, have been shown to reduce the clearance of benzodiazepines and may potentiate their action and known inducers of hepatic enzymes, eg. rifampicin, may increase the clearance of benzodiazepines.

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## Overdosage

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When taken alone in overdosage diazepam presents few problems in management. Signs may include drowsiness, ataxia and dysarthria, with coma in severe cases. Treatment is symptomatic. Gastric lavage is useful only if performed soon after ingestion.

The value of dialysis has not been determined. Flumazenil is a specific IV antidote for use in emergency situations. Patients requiring such intervention should be monitored closely in hospital.

When taken with centrally-acting drugs, especially alcohol, the effects of overdosage are likely to be more severe and, in the absence of supportive measures, may prove fatal.

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## Pharmaceutical Precautions

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The recommended maximum storage temperature for Propam is 25°C. Protect from light.

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## Medicine Classification

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Controlled Drug C5.

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## Package Quantities

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2 mg Tablet: Bottles of 100's and 500's.

5 mg Tablet: Bottles of 100's, 250's & 500's.

10 mg Tablet: Bottles of 100's and 500's.

**Not all pack sizes may be marketed.**

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## **Further Information**

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The elderly, and patients with impaired renal and/or hepatic function, will be particularly susceptible to the adverse effects listed above. It is advisable to review treatment regularly and to discontinue use as soon as possible.

Treatment should be kept to a minimum and given only under close medical supervision. Little is known regarding the efficacy or safety of benzodiazepines in long-term use.

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## **Name and Address**

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## **Date of Preparation**

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2 February 2009