PROFESSIONAL INFORMATION

SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE

MOGADON 5 mg tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each **MOGADON** tablet contains 5 mg nitrazepam.

MOGADON contains 307.5 mg of lactose per tablet.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

White tablet imprinted with ICN on the upper face. The lower face is scored. Diameter 12,0 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Short term relief of insomnia caused primarily by anxiety-related factors.

MOGADON is only indicated when the sleeping disorder is severe, disabling or subjecting the individual to extreme stress.

4.2 Posology and method of administration

Posology

1 tablet (5 mg) before retiring.

This average dosage may if necessary be increased up to 10 mg.

Special populations

Elderly patients: ½ to 1 tablet

Paediatric population

Children

MOGADON tablets are contraindicated for use in children.

Method of administration

MOGADON tablets are for oral administration. The tablet may be swallowed whole, chewed, or dissolved in liquid. Treatment should be as short as possible. Generally, the duration of treatment varies from a few days to two weeks with a maximum, including tapering off process of four weeks. In certain cases, extension beyond the maximum treatment period may be necessary, if so, it should not take place without re-evaluation of the patient's status. **MOGADON** should be withdrawn for a treatment-free period at regular intervals to ascertain whether the therapy needs to be continued. **MOGADON** therapy should not be stopped abruptly, but the dose should be tapered off.

4.3 Contraindications

- Hypersensitivity to nitrazepam or to any of the excipients (see section 6.1)
- Myasthenia gravis
- Hypersensitivity to benzodiazepines including rash, angioedema and hypertension have been reported on rare occasions in susceptible patients.
- Severe respiratory insufficiency, respiratory depression
- Sleep apnoea syndrome
- Severe hepatic insufficiency

- Phobic or obsessional states; chronic psychosis
- Pregnancy and lactation (see section 4.6)
- Use in Children

4.4 Special warnings and precautions for use

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

MOGADON should not be used alone to treat depression or anxiety associated with depression, since suicide may be precipitated in such patients. Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse. Benzodiazepines are not recommended for the primary treatment of psychotic illness.

Concomitant use of **MOGADON** and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of sedative medicines such as benzodiazepines or related drugs such as **MOGADON** with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe **MOGADON** concomitantly with opioids, the lowest effective dose should be used, and the duration of treatment should be as short as possible (see also general dose recommendation in section 4.2).

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers (where applicable) to be aware of these symptoms (see section 4.5).

If the patient is awoken during the period of maximum drug activity, recall may be impaired.

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

There is a potential for abuse and the development of physical and psychic dependence, especially with prolonged use and high doses. The risk of dependence is also greater in patients with a history of alcohol or drug abuse. Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms These may consist of headache, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases, the following symptoms may occur: derealisation, depersonalization, hyperacusis, numbness and tingling of extremeties, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures. Rebound insomnia, a transient syndrome whereby the symptoms that led to treatment with benzodiapepine recur in an enhanced form, may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety and restlessness.
Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage be decreased gradually. Some tolerance to the hypnotic effects of nitrazepam may develop after repeated use.

Pre-existing depression may be unmasked during nitrazepam use.

Particular caution should be exercised in the following instances: elderly and debilitated patients who are at particular risk of over sedation, respiratory depression and ataxia, and the initial dosage should be reduced I these patients; patients with chronic respiratory insufficiency due to the risk of respiratory depression: in infants and young children, as well as elderly, bed-ridden patients,

bronchial hypersecretion and excessive salivation leading to aspiration/pneumonia may occur on rare occasions; patients with impaired renal function or hepatic function: patients suffering from anxiety accompanied by an underlying depressive disorder. Nitrazepam is not recommended for the primary treatment of psychotic illness. Nitrazepam should not be used alone to treat depression or anxiety associated with depression (suicide may be precipitated in such patients): patients receiving barbiturates or other CNS depressants - there is an additive risk of CND depression when these medicines are taken together.

Patients should be cautioned regarding the additive effects of alcohol and **MOGADON.**

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural effects include paradoxical aggressive outbursts, excitement, confusion, restlessness, agitation, irritability, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and the uncovering of depression with suicidal tendencies. Extreme caution should therefore be used in prescribing benzodiazepines to patients with personality disorders. If any of these reactions occur, use of the drug should be discontinued. These reactions may be quite severe and are more likely to occur in the elderly.

Benzodiazepines may induce anterograde amnesia. The condition usually occurs 1 to 2 hours after ingesting the product and may last up to several hours. Therefore, to reduce the risk, patients should ensure that they will be able to have an uninterrupted sleep of 7 to 8 hours.

Due to the myorelaxant effect there is a risk of falls and consequently of hip fractures particularly for elderly patients when they get up at night.

Lactose

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine

4.5 Interaction with other medicines and other forms of interaction

Concomitant intake with alcohol should be avoided. The sedative effect may be enhanced when the product is used in combination with alcohol.

Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics (neuroleptics, hypnotics, anxiolytics/sedatives, antidepressants agents, narcotic analgesics, antiepileptics, anaesthetics and sedative antihistamines.

In the case of narcotic analgesics, enhancement of the euphoria may also occur leading to an increase in psychic dependence.

Compounds which inhibit certain hepatic enzymes (including cytochrome P450) may enhance the activity of nitrazepam.

The concomitant use of sedative medicines such as benzodiazepines or related drugs such as **MOGADON** with opioids increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see section 4.4).

When **MOGADON** 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no evidence as to drug safety in human pregnancy, nor is there evidence from animal work that it is free from hazard. Do not use during pregnancy,

especially during the first and last trimesters, unless there are compelling reasons. Given during labour **MOGADON** crosses placenta and may cause the "floppy-infant" syndrome characterized by central respiratory depression, hypothermia, hypotonia and poor sucking. Moreover, infants born to mothers who took nitrazepam chronically during the latter stages of pregnancy, may have developed physical dependence and may be at some risk of developing withdrawal symptoms in the postnatal period.

Breastfeeding

Since benzodiazepines are found in the breast milk, the use of nitrazepam in mothers who are breast-feeding should be avoided.

4.7 Effects on ability to drive and use machines

Patients should be advised that, like all medicines of this type, **MOGADON** Tablets may modify patients' performance at skilled tasks. Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or use machinery. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased. Patients should further be advised that alcohol may intensify any impairment and should therefore be avoided during treatment.

This medicine can impair cognitive function and can affect a patient's ability to drive safely.

4.8 Undesirable effects

a. Summary of the safety profile

Undesirable effects that may occur are drowsiness during the day, numbed emotions, confusion, fatigue, headache, dizziness, muscle weakness, ataxia, or

double vision. These phenomena occur predominantly at the start of therapy and usually disappear with repeated administration.

Other side-effects like gastrointestinal disturbances, changes in libido, skin reactions or amnesia have been reported occasionally.

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reactions**
Blood and lymphatic system disorders	Frequency not known:	Blood disorder
Immune system disorders	Frequency not known:	Allergic skin reaction, anaphylactic reaction, angioedema
Psychiatric disorders	Common:	Numbed emotions, confusion state, depression (pre-existing depression may be unmasked).
	Rare:	Libido disorder
	Frequency not known:	Emotional disorder, delirium, insomnia, cognitive impairment, physical and psychological dependence (even at therapeutic doses), withdrawal syndrome accompanied by reactions including mood changes, anxiety, and restlessness, drug abuse, agitation, aggression, delusion, anger, nightmare, hallucination, psychotic disorder.

MedDRA system organ class	**Frequency**	**Adverse reactions**
Nervous system disorders	Common:	Drowsiness, reduced alertness, headache, dizziness
	Rare:	Vertigo
	Frequently not known:	Balance disorder, hypokinesia, tremor, enterograde, amnesia, epilepsy
Eye disorders	Common:	Diplopia
	Rare:	Visual impairments
Vascular disorders	Rare:	Hypotension
Respiratory, thoracic and mediastinal disorders	Frequency not known:	Respiratory depression, increased bronchial secretion
Gastrointestinal disorders	Rare:	Abdominal discomfort
Hepato-biliary disorders	Frequency not known:	Jaundice
Skin and subcutaneous tissue disorders	Rare:	Skin rashes
	Frequency not known:	Urticaria, pruritus, dermatitis, erythema multiforme, Stevens-Johnson syndrome
Musculoskeletal and connective tissue disorders	Common:	Muscle weakness
	Frequency not known:	Muscle spasm
Renal and urinary disorders	Rare:	Urinary retention
General disorders and	Common:	Fatigue, ataxia

MedDRA system organ class	Frequency	Adverse reactions
administration site conditions	Frequency not known:	Irritability, rebound effect

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms:

Overdosage of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion, dysarthria and lethargy; in more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, rarely coma and very rarely death

Suggested treatment of overdosage:

1. Vomiting should be induced (within 1 hour) if the patient is conscious or gastric lavage can be performed (up to 2 hours after ingestion) if the patient is unconscious. If there is an advantage in emptying the stomach, activated charcoal should be given to reduce absorption. Special attention should be paid to

respiratory and cardiovascular functions in intensive care. The value of dialysis has not been determined.

2. Flumazenil may be used to reverse central sedative effects of benzodiazepines. Flumazenil is a specific IV antidote for use in emergency situations. Patients requiring such intervention should be monitored closely in hospital. The benzodiazepine antagonist flumazenil is not indicated in patients with epilepsy who have been treated with benzodiazepines. Antagonism of the benzodiazepine effect in such patients may trigger seizures. If excitation occurs, barbiturates should not be used.

3. Recovery is usually uneventful, even without active therapy although continuous observation is suggested because of the possibility of vomiting followed by suffocation due to inhalation.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category A:2.2 - Sedatives, Hypnotics, ATC Code: N05CD02

MOGADON induces sleep by its inhibitory action on the structures of the limbic system. It is suggested that, although benzodiazepine binding sites are also found in other organs, their density is highest in the central nervous system, particularly in cortical and limbic-forebrain areas. The affinity of a given benzodiazepine for such receptor sites approximately parallels its pharmacologic potency both in animals and in human beings.

The net effect of the interaction with receptors is to enhance the inhibitory neuronal properties of the neurotransmitter gamma-aminobutyric acid (GABA).

5.2 Pharmacokinetic properties

Absorption

Nitrazepam is absorbed from the gastro-intestinal tract. the degree of absorption being subject to individual variation (60-90 %). Two hours after administration, the concentration of nitrazepam in the cerebrospinal fluid is about 8 % and after 36 hours approximately 16 % of the concentration in the plasma. The CSF concentration thus corresponds to the non-protein-bound fraction of active ingredient in the plasma.

Distribution

In younger persons the volume of distribution is 2 L/kg, in elderly patients the volume of distribution is greater, and the mean elimination half-life rises to 40 hours.

Biotransformation

Nitrazepam undergoes biotransformation to a number of metabolites, none of which possess significant clinical activity.

Elimination

The elimination of nitrazepam from the blood is biphasic. Only a small percentage of oral dose of **MOGADON** appears in the urine as unchanged nitrazepam. The active ingredient is reduced in the liver to the 7-amino compound, which is metabolized in turn to 7-acetamidonitrazepam in elderly patients. Similar tendencies can be expected in patients with impaired liver function. Nitrazepam passes through the placental barrier and enters the milk of nursing mother.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose

Maize Starch

Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

60 months

6.4 Special precautions for storage

Store at or below 25 ˚C.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

PVC/PVDC foil and Aluminium foil blister packs, containing 30 tablets.

6.6 Special precautions for disposal

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

Trinity Pharma (Pty) Ltd

106 16th Road

Midrand

1686

8 REGISTRATION NUMBER(S)

B1005 (Act 101/1965)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23 February 1996

10 DATE OF REVISION OF THE TEXT

26 October 2022