SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Remnos 5 mg Tablets
Nitrazepam 5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Nitrazepam 5.00 mg

Excipient(s) with known effect

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

4.1 Therapeutic indications

Adults: Short term treatment of insomnia only when it is severe, disabling, or subjecting the individual to extreme distress. An underlying cause for insomnia should be sought before deciding on the use of benzodiazepines for symptomatic relief.

Children: Not recommended.

4.2 Posology and method of administration

Prior to starting treatment with Nitrazepam, a discussion should be held with patients to put in place a strategy for ending treatment with Nitrazepam in order to minimise the risk of dependence, addiction and drug withdrawal syndrome (see section 4.4).

Treatment should be given for the shortest possible duration.

Adults: The dosage may vary according to the patient's response and the severity of the insomnia. The recommended dose is 5 mg before retiring. This, however, may be increased to 10 mg.

The lowest dose which can control symptoms should be used. It should not be continued beyond 4 weeks.
Long term chronic use is not recommended.
Treatment should always be tapered off gradually.

Patients who have taken benzodiazepines for a long time may require a longer period during which the doses are reduced.

Elderly: Half the normal adult dose may be sufficient for a therapeutic response in the elderly. (See Warnings and Adverse Effects).

Children: Not recommended

Route of Administration: Oral

4.3 Contraindications

- Known sensitivity to benzodiazepines.
- Acute pulmonary insufficiency.
- Respiratory depression.
- Chronic psychosis.
- Phobic or obsessional states.
- Myasthenia gravis.
- Sleep apnoea syndrome.
- Severe hepatic insufficiency.
- Acute porphyria.

4.4 Special warnings and precautions for use

Chronic pulmonary insufficiency. In chronic renal or hepatic disease. In labour. High single doses or repeated low doses have been reported to produce hypotonia, poor suckling and hypothermia in the neonate and irregularities in the foetal heart.

The use of benzodiazepines may lead to development of physical and psychological dependency upon these agents. The risk of dependence is greater the higher the dose and the longer the duration of treatment and in patients with a history of alcoholism or drug abuse. In such cases, benzodiazepines should be used with extreme caution, the patient should be regularly monitored, routine repeat prescriptions avoided and treatment should be withdrawn gradually.

Drug dependence, tolerance and potential for abuse

Drug addiction comprises behavioural, cognitive and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use and possible tolerance or physical dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, which manifests as withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug. Addiction and dependence are related but distinct presentations and in discussing these themes, terminology that apportion blame to the individual should be avoided.

For all patients, prolonged use of this product may lead to drug dependence and addiction but can occur with short-term use at recommended therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of drug misuse.
A comprehensive patient history should be taken to document concomitant medications, including over-the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.
Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of symptom control as initially experienced. Patients may also supplement their treatment with additional medications to achieve the same effect. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.
Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.
Patients should be closely monitored for signs of misuse, abuse, or addiction.
The clinical need for treatment with Nitrazepam should be reviewed regularly, with frequent assessments of patients being undertaken during the course of their treatment.
Drug withdrawal syndrome
Prior to starting treatment with Nitrazepam, a discussion should be held with patients to explain the risk of dependence, addiction, and drug withdrawal syndrome. A withdrawal strategy for ending treatment with Nitrazepam should also be put in place with the patient before starting treatment (there may be exceptions to this in specific clinical situations such as symptom management in end of life palliative care).
Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take in excess of weeks or months. Patients should be informed of this when the medication is first prescribed.
The reduction schedule for a patient should be tailored to the individual and should be modified to allow intolerable withdrawal symptoms to improve before making the next reduction. If using a published withdrawal schedule, apply it flexibly to accommodate the person's preferences, changes to their circumstances and the response to dose reductions.
Suggest a slow stepwise rate of reduction proportionate to the existing dose, so that decrements become smaller as the dose is lowered, unless clinical risk is such that rapid withdrawal is needed.
If a patient develops withdrawal reactions, consider pausing the taper or increasing the dosage to the previous tapered dosage level.
If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.
Depression, nervousness, irritability, rebound insomnia, sweating, panic attacks, dysphoria and diarrhoea have been reported after abrupt withdrawal of treatment even in patients who received normal therapeutic doses for a short time. In rare cases withdrawal following excessive doses may produce convulsions, confusional states and psychotic disorders.
Extreme caution should be used in prescribing benzodiazepines to patients with personality disorders.

Benzodiazepines may inhibit psychological adjustment in cases of loss or bereavement.
Duration of treatment should be as short as possible. It should not exceed four weeks including the tapering off process. Treatment should not extend beyond four weeks without re-evaluation of the situation.

4.5 Interaction with other medicinal products and other forms of interaction

If Nitrazepam is combined with alcohol or with centrally active drugs such as neuroleptics, tranquillisers, hypnotics, anti-depressants, analgesics and anaesthetics, the sedative effects are likely to be intensified.

Enhanced central depressive effect may occur when benzodiazepines are given concomitantly with anti psychotics (neuroleptics), narcotic analgesics, antidepressants, hypnotic, anaesthetics and sedative antihistamines. In the case of narcotic analgesics, enhancement of euphoria may also occur, leading to an increase in psychic dependence.

Cimetidine inhibits the metabolism of many benzodiazepines and may potentiate their action.

Omeprazole and isoniazid inhibit diazepam metabolism, and that of other benzodiazepines.

Rifampicin may increase clearance of nitrazepam.

Concurrent use of zidovudine with benzodiazepines may decrease zidovudine clearance.

The sedative effect of benzodiazepines is enhanced when taken in combination with alcohol. Concomitant intake should be avoided.

Both depression and the elevation of drug levels, as well as no change in levels have been reported when diazepam is taken in combination with anti-epileptics. Side-effects and toxicity may be more evidence, particularly when barbiturate and hydantoins or combinations including them are taken in conjunction with diazepam. Nitrazepam may also interact similarly.

4.6 Fertility, pregnancy and lactation

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

4.7 Effects on ability to drive and use machines

Sedation, impaired concentration, ataxia and amnesia may occur with nitrazepam and adversely affect ability to drive or operate machinery. Alcohol may intensify such effects and should be avoided during treatment. Drowsiness may persist the next day and affect performance at skilled tasks.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
  - the medicine has been prescribed to treat a medical or dental problem and;
  - you have taken it according to the instructions given by the prescriber and in the information provided with the medicine and;
  - it was not affecting your ability to drive safely

4.8 Undesirable effects

Not for use in phobic or obsessional states because there is inadequate evidence of efficacy and safety.
Should not be used alone to treat depression or anxiety associated with depression. (Suicide may be precipitated in such patients).
Not to be used for treatment of chronic psychosis.
Amnesia may occur. In cases of loss or bereavement psychological adjustment may be inhibited by benzodiazepines.
Not to be used for the treatment of chronic psychosis.
Disinhibiting effects may be manifested in various ways. Suicide may be precipitated in patients who are depressed and aggressive behaviour toward self and others may be precipitated. Extreme caution should therefore be used in prescribing benzodiazepines in patients with personality disorders.

<u>Psychiatric disorders:</u>

Drug dependence (see section 4.4)

<u>General disorders and administration site conditions:</u>

Drug withdrawal symptoms (see 4.4 Special warnings and precautions).

Symptoms reported following discontinuation of benzodiazepines include headaches, muscle pain, anxiety, tension, depression, insomnia, restlessness, confusion, irritability, sweating, and the occurrence of "rebound" phenomena whereby the symptoms that led to treatment with benzodiazepines recur in an enhanced form. These symptoms may be difficult to distinguish from the original symptoms for which the drug was prescribed.

In severe cases the following symptoms may occur: derealisation; depersonalisation; hyperacusis; tinnitus; numbness and tingling of the extremities; hypersensitivity to light, noise, and physical contact; involuntary movements; hyperreflexia, tremor, nausea, vomiting; diarrhoea, abdominal cramps, loss of appetite, agitation, palpitations, tachycardia, panic attacks, vertigo, short-term memory loss, hallucinations/delirium; catatonia; hyperthermia, convulsions. Convulsions may be more common in patients with pre-existing seizure disorders or who are taking other drugs that lower the convulsive threshold such as antidepressants.

Withdrawal from benzodiazepines may be associated with physiological and psychological symptoms of withdrawal including depression.
Withdrawal symptoms occur with benzodiazepines following normal therapeutic doses for short periods of time.
Dose-related adverse effects which occur commonly with nitrazepam and which may persist into the following day, even after a single dose include sedation, drowsiness, unsteadiness, and ataxia (especially in the elderly).
The elderly are particularly sensitive to the effects of centrally-depressant drugs and experience confusion, especially if organic brain changes are present.
Less commonly, headache, vertigo, hypotension, gastro-intestinal disturbances, skin rashes, changes in libido and urinary retention have been reported. Isolated cases of blood dyscrasias and jaundice have been reported.
Abnormal psychological reactions have been reported and are more likely to occur in children and the elderly. Rare behavioural effects include excitement, confusion, paradoxical aggressive outbursts and unmasking of depression with suicidal tendencies. If these occur, nitrazepam should be discontinued.
Nitrazepam should not be used alone to treat depression or anxiety associated with depression, since suicide may be precipitated in such patients.
Benzodiazepines may induce antegrade amnesia which occurs most often several hours after ingesting the drug. Amnesic effects may be associated with inappropriate behaviour.
Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.

Symptoms of nitrazepam overdosage are mainly an intensification of its therapeutic effects - sedation, muscle weakness, profound sleep or paradoxical excitation. In more severe cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression and rarely, coma and death. When combined with other CNS depressants, including alcohol, the effects of overdosage are likely to be more severe and may prove fatal.
Treatment of overdosage includes induction of emesis within one hour, if the patient is conscious. If the patient is unconscious, gastric lavage should be undertaken with the airways protected. Activated charcoal should be administered to reduce absorption. Respiratory and cardiovascular functions should be carefully monitored in intensive care. If excitation occurs, barbiturates should not be used. Flumazenil, a specific competitive inhibitor of the central effects of benzodiazepines, may be useful as an antidote but expert advice is essential since adverse effects may occur (e.g. convulsions in patients dependent on benzodiazepines). Benzodiazepines are not significantly removed from the body by dialysis.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Central Nerous System depressant acting on benzodiazepine receptors.

ATC code: N05CD02

5.2 Pharmacokinetic properties

1. Half-life: 18-28 hours.
2. Absorbed from gastro-intestinal tract and maximum plasma concentration is reached in 2 hours.
3. About 5% excreted unchanged in the urine together with the metabolites 7-amino and 7-acetylamino metabolites in the first 48 hours.

Also excreted in the milk of lactating mothers.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize Starch
Pregelatinised Maize Starch
Ethylcellulose 100 cps
Magnesium Stearate

6.2 Incompatibilities

There are no known major incompatibilities.

6.3 Shelf life

36 months all pack sizes

6.4 Special precautions for storage

Keep container well closed, in a dry place, below 25°C.

6.5 Nature and contents of container

Polypropylene or high density polystyrene with polythene closures and polyurethane wads or polythene inserts. Pack sizes: 100, 500

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special instructions.

7 MARKETING AUTHORISATION HOLDER

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PL 33414/0068

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31/12/2025