NITRAPAM TABLETS 5MG

NAME AND STRENGTH OF ACTIVE SUBSTANCE:
Each tablet contains:
Nitrazepam……5mg

PRODUCT DESCRIPTION:
A blue, round, flat of 11mm diameter tablet with 'MPI' logo.

PHARMACODYNAMICS :
Nitrazepam is a benzodiazepine hypnotic which enhances or facilitates the inhibitory neurotransmitter action of gamma-aminobutyric acid (GABA) receptors. It mediates both pre- and post-synaptic inhibition in all regions in the central nervous system, following interaction between the benzodiazepine and a specific neuronal membrane receptor.

PHARMACOKINETICS:
Nitrazepam is 80% bioavailable after oral administration. Peak concentrations are reached in 0.5 to 5 hours. It is widely distributed in the body; 10 to 15% is found in cerebrospinal fluid and 85 to 90% is bound to plasma proteins. It also crosses the placenta and is found in breast milk. It is extensively metabolized to inactive substances that are excreted in the urine. The elimination half-life is approximately 30 hours.

INDICATION:
Nitrazepam is a benzodiazepine widely used as a sedative/hypnotic and in the management of myoclonic seizures.

RECOMMENDED DOSAGE:
Adults: as hypnotic the usual dose is 5 to 10mg at night
Children: dosage in children up to 12 years is not established.

ROUTE OF ADMINISTRATION:
To be taken orally.

CONTRAINDICATIONS:
It is contraindicated in patients with acute narrow angle glaucoma.

WARNINGS AND PRECAUTIONS:
1. Abrupt drug withdrawal may result in rebound insomia, an abstinence syndrome similar to barbiturate withdrawal seizures or rarely, psychosis
2. Use with caution in patient with impaired hepatic function.
3. Nitrazepam should be used with caution in patient with chronic obstructive lung disease or respiratory failure.
4. This preparation may be habit forming on prolonged use.
5. Anaphylaxis (severe allergic reaction) and angioedema (severe facial swelling) which can occur as early as the first time the product is taken.
6. Complex sleep-related behaviour which may include sleep driving, making phone calls, preparing and eating food while asleep.
7. Nitrazepam causes drowsiness and these effects are enhanced by the simultaneous administration of depressants such as alcohol.
8. Risk from concomitant use with opioids:
   Profound sedation, respiratory depression, coma, and death may result from the concomitant use of Nitrapam Tablets 5mg with opioids. Observational studies have demonstrated that concomitant use of opioids and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
   If the decision is made to newly prescribe a benzodiazepine and an opioid together, prescribe the lowest effective dosages and minimum durations of concomitant use.
   If the decision is made to prescribe a benzodiazepine in a patient already receiving an opioid, prescribe a lower initial dose of the benzodiazepine than indicated in the absence of an opioid, and titrate based on clinical response.
   If the decision is made to prescribe an opioid in a patient already taking a benzodiazepine, prescribe a lower initial dose of the opioid, and titrate based on clinical response.
   Follow patients closely for signs and symptoms of respiratory depression and sedation. Advise both patients and caregivers about the risks of respiratory depression and sedation when Nitrapam Tablets 5mg is used with opioids. Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the opioid have been

determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of opioids (See Drug Interactions).

INTERACTIONS WITH OTHER MEDICAMENTS:

CNS depressants, other, such as alcohol, analgesics, general anaesthetics and tricyclic antidepressants - concurrent use may increase the effects of either these medications or benzodiazepines; when a benzodiazepine is used concurrently with a narcotic analgesic, the dosage of narcotic should be reduced by at least one-third and administered in small increment.

Opioids: Due to additive pharmacologic effect, the concomitant use of opioids with benzodiazepines increases the risk of respiratory depression, profound sedation, coma and death.

The concomitant use of opioids and benzodiazepines increases the risk of respiratory depression because of actions at different receptor sites in the central nervous system that control respiration. Opioids interact primarily at μ-receptors, and benzodiazepines interact at $GABA_A$ sites. When opioids and benzodiazepines are combined, the potential for benzodiazepines to significantly worsen opioid-related respiratory depression exists.

Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate (see Warnings and Precautions).

Limit dosage and duration of concomitant use of benzodiazepines and opioids, and follow patients closely for respiratory depression and sedation.

PREGNANCY AND LACTATION:

Nitrazepam crosses the placenta and is excreted in breast milk. Use with caution during pregnancy and in nursing women.

SIDE EFFECTS:

1. Drowsiness, light-headedness, and ataxia are the most common and are often dose-dependent. Elderly and debilitated patients are especially susceptible to these reactions.
2. Other effects occasionally observed includes hypotension, some respiratory depression, nausea and constipation, changes in salivation, blurred vision and diplopia, dysarthria, skin rashes, urinary retention, incontinence, mental depression, tremor, headache, confusion, slurred speech, vertigo and changes in libido.
3. Rarely, hepatic disease and blood dyscrasias occur.

SYMPTOMS AND TREATMENT OF OVERDOSAGE:

If overdosage occurs, the stomach should be emptied by aspiration and lavage. IV fluid should be administered and an adequate airway maintained.

EFFECT ON ABILITY TO DRIVE AND USE MACHINE.

Can cause drowsiness. Do not drive and use machine.

PRECLINICAL SAFETY DATA

Not applicable

INSTRUCTION FOR USE

For oral use only

DOSAGE FORMS AND PACKAGING AVAILABLE:

Dosage Form: Tablet
Pack size:Blister pack: 100 x 10’s

NAME AND ADDRESS OF MANUFACTURER / PRODUCT REGISTRATION HOLDER:

MALAYSIAN PHARMACEUTICAL INDUSTRIES SDN BHD (101323-U)
Plot 14, Lebuhraya Kampung Jawa,11900 Bayan Lepas,
Pulau Pinang, Malaysia.

DATE OF REVISION:

22/01/2019