XANAPAM TABLETS 0.5MG
XANAPAM TABLETS 1MG

NAME AND STRENGTH OF ACTIVE SUBSTANCE:

XANAPAM TABLETS 0.5MG

Each tablet contains:

Alprazolam……0.5mg

XANAPAM TABLETS 1MG

Each tablet contains:

Alprazolam……1mg

PRODUCT DESCRIPTION:

XANAPAM TABLETS 0.5MG

A pink, scored, flat, oval tablet of 7.7x5.25mm

XANAPAM TABLETS 1MG

A blue, scored, flat, oval tablet of 7.7x5.25mm.

PHARMACODYNAMICS:

Alprazolam is a benzodiazepine 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. Alprazolam is shorter acting than diazepam and thus have more severe withdrawal syndromes. A role for the platelet-activating factors (PAF) has also been postulated.

PHARMACOKINETICS:

Alprazolam is rapidly and completely absorbed from the gastro-intestinal tract following oral administration with peak plasma concentrations of one to two hours after a dose. The plasma half-lives of alprazolam are 12 to 15 hours. It is 70-80% bound to plasma protein. Metabolism of the drug occurs mainly in the liver, metabolizing it to a-hydroxyalprazolam, which is half as active as the parent compound, and also to the inactive benzophenone. It is excreted as unchanged drugs and its metabolites renally.

INDICATION:

Alprazolam shares the actions of other benzodiazepines and is used for the management of anxiety disorders or the short term relief of anxiety or anxiety associated with depressive symptoms. Alprazolam is also used in the management of panic disorder, with or without agrophobia.

RECOMMENDED DOSAGE:

The general principal of using the lowest effective dosage should be followed, especially those who have not previously been treated with minor tranquilizers, antidepressants, hypnotics or those with a history of chronic alcoholism, in order to achieve the therapeutic effects. When a higher dose is required, the evening dose should be increased before the day time doses.

If side effects occur, the dose should be lowered. On discontinuation of therapy, the dosage should be tapered off gradually. Patients who have taken benzodiazepines for a long time may require longer period during which doses are reduced.

The recommended doses are given below:

	Usual starting dose	Usual dosage range
Anxiety	0.25 to 0.5mg, given three times daily.	0.5 to 4.0mg daily, given in divided doses.
Depression	0.5mg, given three times daily.	1.5 to 4.5mg daily, given in divided doses.
Elderly or debilitating patients	0.25mg, given two or three times daily.	0.5 to 0.75mg daily, given in divided doses.
Panic-related disorder	0.5 to 1mg, given at bedtime or 0.5mg three times daily.	The dose should be adjusted to patient's response. Dosage adjustment should be in increment no greater than 1mg every 3 to 4 days. Additional doses can be added until a three or four times daily dose is achieved. Maximum dose is 10mg daily.

ROUTE OF ADMINISTRATION:
To be taken orally.

CONTRAINDICATIONS:
It is contraindicated in patients with respiratory depression, acute pulmonary insufficiency and severe hepatic impairment. It is not recommended for phobic, obsessional states and chronic psychosis.
Known hypersensitivity and history of allergy to alprazolam.
Alprazolam should not be used to treat short term mild anxiety such as anxiety or tension associated with the stress of everyday life. It should not be used for long term chronic treatment.

WARNINGS AND PRECAUTIONS:
1. This preparation may be habit forming on prolonged use.
2. Clinicians should be aware of the possible hepatotoxicity, especially when used in combination with MAOI.
3. Safety and efficacy of alprazolam have not been established in children younger than 18 years of age.
4. Alprazolam, in common with other benzodiazepines which undergo oxidation metabolism, would accumulate to a greater extent in patients with alcoholic liver disease than in healthy subjects. The daily doses of alprazolam may need to be reduced by half in this population.
5. Precaution should be taken when used in patient with impaired renal function.
6. Anaphylaxis (severe allergic reaction) and angioedema (severe facial swelling) which can occur as early as the first time the product is taken.
7. Complex sleep-related behaviours which may include sleep driving, making phone calls, preparing and eating food (while asleep).
8. This product may cause drowsiness. Avoid alcoholic beverages.
9. Risk from concomitant use with opioids:
   Profound sedation, respiratory depression, coma, and death may result from the concomitant use of Xanapam 0.5mg / 1mg 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 Xanapam 0.5mg / 1mg 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. Enhanced sedation or respiratory and cardiovascular depression may occur if alprazolam is given with other CNS depressants.
Antidepressants. Alprazolam has been reported to increase the steady-state plasma concentrations of imipramine and desipramine. However, the clinical significance of such changes is unknown.
Antiepileptics. The metabolism of alprazolam may be enhanced by long term therapy with hepatic enzyme inducers such as carbamazepine, phenobarbitone and phenytoin. The half-lives have been shorted and the clearance will be increased.
H antagonist. Cimetidine has been reported to inhibit the metabolism of alprazolam.
Disulfiram. Patients should be closely observed for the evidence of enhanced benzodiazepines response during concomitant therapy with disulfiram.
Antifungal. Antifungal agent such as ketoconazole which undergo oxidative metabolism may decrease benzodiazepines plasma clearance and increased plasma half-lives and concentrations of these benzodiazepines. Increased sedative effect may be observed in patients receiving concomitant therapy with a benzodiazepine and antifungal agent.
Erythromycin. Concomitant use of erythromycin and alprazolam may decrease clearance of alprazolam and could increase the pharmacologic effects of the drug.
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:
It should be avoided during the period of pregnancy and lactation.

SIDE EFFECTS:
Common side effects include drowsiness, light-headedness the next day, confusion and ataxia (especially in elderly), amnesia, dependence, rashes, changes in libido, blood disorder, jaundice, and urinary retention.
Less common side effects include blurred vision, coordination disorder, headache, vertigo, hypotension, salivation changes and gastro-intestinal disturbances.
As with other benzodiazepines, paradoxical reactions such as hallucinations, confusion, agitation, stimulation or other behavioural effects may occur in rare instances.

SYMPTOMS AND TREATMENT OF OVERDOSAGE:
Symptoms: Indicators of overdosage include ataxia, somnolence, impaired coordination, slurred speech, confusion, coma and diminished reflexes. Other symptoms such as hypotension, seizures, respiratory depression and apnea may also occur. Death from overdosage in the absence or concurrent use of alcohol is rare. Most patients recover rapidly.

Treatment: Overdosage should be treated by inducing vomiting and/or gastric lavage. Activated charcoal and a saline cathartic may also be used after gastric lavage or emesis to remove the remaining drug. Flumazenil (benzodiazepine antagonist) may also be useful in the diagnosis of overdosage. Respiration, pulse and blood pressure should be monitored and supported by general measures when necessary. As the management of overdosage, physician should bear in mind that multiple agents may have been ingested. Hypotension may be controlled by IV infusion of noradrenaline or metaraminol if necessary.

EFFECT ON ABILITY TO DRIVE AND USE MACHINE.
Can cause drowsiness. Do not drive or operate machinery.

PRECLINICAL SAFETY DATA
Not applicable

INSTRUCTION FOR USE
For oral use only

DOSAGE FORMS AND PACKAGING AVAILABLE:
Dosage Form: Tablet
XANAPAM TABLETS 0.5MG
Packing size: Blister pack: 50 x 10's
XANAPAM TABLETS 1MG
Packing size: Blister pack: 50 x 10's

NAME AND ADDRESS OF MANUFACTURER / PRODUCT REGISTRATION HOLDER:
MALAYSIAN PHARMACEUTICAL INDUSTRIES SDN BHD (101323-U)
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DATE OF REVISION:
29/05/2019