

DATA SHEET

OX-PAM

Oxazepam 10mg and 15mg tablets.

Presentation

10mg Tablet: White, round, flat tablet having a diameter of 7.94mm and a bisecting score on one side.

15mg Tablet: Yellow, round, flat tablet having a diameter of 7.94mm and a bisecting score on one side.

Uses

Actions

Oxazepam is a benzodiazepine compound having anti-convulsant, sedative, muscle relaxant and amnesic properties.

In general, benzodiazepines act as depressants of the central nervous system (CNS), producing all levels of CNS depression from mild sedation to hypnosis to coma depending on dose.

The precise sites and mechanisms of action have not been completely established.

Although various mechanisms of action have been proposed, it is believed that benzodiazepines enhance or facilitate the inhibitory neurotransmitter action of gamma-aminobutyric acid (GABA), which is one of the major inhibitory neurotransmitters in the brain and mediates both pre- and post-synaptic inhibition in all regions of the CNS, following interaction between the benzodiazepine and a specific neuronal membrane receptor.

Benzodiazepines reportedly act as agonists at the benzodiazepine receptors, which have been shown to form a component of the benzodiazepine-GABA-receptor-chloride ionophore complex. Most anxiolytics appear to act through at least one of the components of this complex to enhance the inhibitory action of GABA. Other actions of benzodiazepines, such as sedative, anticonvulsant and muscle relaxant effects, may be mediated through a similar mechanism, although different receptor subtypes may be involved.

Pharmacokinetics

Oxazepam is well absorbed from the gastrointestinal tract and reaches peak plasma concentrations about 2 hours after ingestion.

Oxazepam is about 85-97% bound to plasma protein and has been reported to have an elimination half life ranging from about 3 to 21 hours. It is largely metabolised to the inactive glucuronide which is excreted in the urine.

During multiple dosage, accumulation is minimal and a steady-state plasma concentration is usually attained within a few days after initiation of therapy. Following termination of treatment, blood concentrations are subclinical in 24 hours and return rapidly to zero (in about four days).

After single oral doses, onset of action depends largely upon absorption rate. After multiple doses, effects depend partly upon rate and extent of medicine accumulation, which in turn relate to elimination half-life and clearance.

Indications

Oxazepam is indicated for the treatment of anxiety, especially anxiety associated with mental depression and for the relief of acute alcohol withdrawal symptoms.

Dosage and Administration

For oral administration.

10mg to 30mg three to four times daily. In elderly or debilitated patients 10mg three to four times daily.

Contraindications

Benzodiazepines are contraindicated where there is acute alcohol intoxication, coma, shock, a history of drug abuse or dependence, acute closed-angle glaucoma, hepatic function impairment (minimal risk), hyperkinesia, hypoalbuminaemia, intolerance to the benzodiazepine prescribed, severe mental depression, myasthenia gravis, organic brain disorders, psychoses, pulmonary disease, renal function impairment, or suicidal tendencies.

Warnings and Precautions

Care may be needed in epileptic patients, in whom the initiation or abrupt withdrawal of benzodiazepine therapy has occasionally provoked seizures.

Prolonged use of oxazepam may lead to development of dependence of the barbiturate-alcohol type. This type of dependence is characterised by: a strong need to continue taking the medicine associated with a tendency to increase the dose, a psychic

dependence on the effects of the medicine and a physical dependence on the effects of the medicine for maintenance of homeostasis.

Oxazepam may give a positive result for the laboratory estimation of glucose.

Oxazepam may enhance the effects of other CNS depressants and alcohol.

Oxazepam likely to produce minor or moderate adverse effects on the stability to drive or use machinery.

Caution is required when giving oxazepam to elderly or debilitated patients. Care should also be exercised in patients with arteriosclerosis, renal, hepatic or respiratory dysfunction.

Withdrawal of oxazepam from patients who have been receiving it in high dose or for a long duration should be gradual.

Mutagenicity: Studies on the mutagenic potential of oxazepam have not been done.

Use in Pregnancy:

Category C

Benzodiazepines may cause hypotonia, respiratory depression and hypothermia in the newborn infant if used in high doses during labour. Withdrawal symptoms in newborn infants have been reported with prolonged use of this class of drugs.

Oxazepam may cross the placenta. There may be a risk of congenital malformations during the first trimester of pregnancy. Risk-benefit must be carefully considered. Chronic usage of benzodiazepines during pregnancy may cause physical dependence with resulting withdrawal symptoms in the neonate. Use of benzodiazepine hypnotics during the last weeks of pregnancy may result in neonatal CNS depression.

Use of benzodiazepines just prior to or during labour may cause neonatal flaccidity.

Use in Lactation: Oxazepam may be excreted in breast milk. Since neonates metabolise benzodiazepines more slowly than adults and accumulation of the benzodiazepine and/or its metabolites may occur, use by nursing mothers may cause sedation, and possibly feeding difficulties and weight loss in the infant. If oxazepam is required by a nursing mother, an alternate method of infant feeding should be used.

Use in Children: Children, especially the very young, are usually more sensitive to the CNS effects of benzodiazepines. Prolonged CNS depression may be produced in the neonate because of inability to biotransform the benzodiazepine into inactive metabolites.

Use in the Elderly: Geriatric patients are usually more sensitive to the CNS effects of benzodiazepines. It is recommended that dosage be limited to the smallest effective dose and increased gradually, if necessary, to decrease the possibility of development of ataxia, dizziness and oversedation.

Adverse Effects

These are usually mild and infrequent. The most common reactions are drowsiness, light-headedness and ataxia. Effects occasionally observed include hypotension, nausea, constipation, blurred vision with changes in colour vision, skin rash, urinary retention, incontinence and central nervous depression and coma.

Oxazepam may, however, paradoxically provoke excitement and dysphoria. Abrupt withdrawal of oxazepam after prolonged use may cause an abstinence syndrome characterised by: apprehension and weakness, anxiety, headache, dizziness, abdominal cramps, insomnia and tachycardia.

Interactions

Oxazepam has the potential to interact with the following:

- Other addictive medications: Prolonged concurrent use may increase the risk of habituation.
- Alcohol and CNS depression-producing medications: Increased CNS depressant effects.
- Tricyclic antidepressants: Possible increase of CNS depressant effects.
- Carbamazepine: Causes decreased metabolism of hepatically metabolised benzodiazepines.
- Levodopa: Concurrent use may decrease the therapeutic effects of levodopa.
- Magnesium sulphate, parenteral: Concurrent use may potentiate the CNS depressant effects of benzodiazepine hypnotics.
- Probenecid: Concurrent use may impair glucuronide conjugation of oxazepam resulting in increased effects and possibly excessive sedation.
- Zidovudine: Concurrent use may competitively inhibit hepatic glucuronisation and decrease the clearance of zidovudine, thereby potentiating the toxicity of zidovudine.

Overdosage

Following an overdosage the stomach may be emptied by gastric lavage and aspiration. Patients should be managed with intensive symptomatic and supportive therapy, with particular attention being paid to the maintenance of cardiovascular, respiratory, and renal functions, and to the maintenance of the electrolyte balance.

Dialysis is of little or no value in poisoning by benzodiazepines.

Pharmaceutical Precautions

36 months from date of manufacture stored at or below 25°C protect from light. Keep out of reach of children.

Medicine Classification

Controlled Drug C5.

Package Quantities

10mg and 15mg tablets: 100s.

Further Information

Oxazepam is 7-Chloro-1,3-dihydro-3-hydroxy-5-phenyl-1,4-benzodiazepin-2-one. Its molecular formula and weight are $C_{15}H_{11}ClN_2O_2$ and 286.7 respectively.

Other ingredients of the tablets are:

10mg tablets: Maize cornflour, Lactose and Magnesium stearate.

15mg tablets: Maize cornflour, Lactose, Magnesium stearate, D&C Yellow No 10 and Sunset Yellow FCF Aluminium lake.

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