DEHYDRATED ALCOHOL BP

Ethanol

Presentation

Dehydrated alcohol BP is a clear, colourless, sterile solution containing not less than 99.4% v/v or 99.0% w/w of ethanol.

Uses

Actions

Ethanol is a central nervous system depressant, which decreases the activity of neurones. Low to moderate blood levels of ethanol depress cortical function, causing an apparent stimulant effect, with loss of judgment, emotional lability, muscle incoordination, visual impairment, slurred speech and ataxia. Ethanol also depresses medullary action, resulting in lethargy, amnesia, hypothermia, hypoglycaemia (especially in children), stupor, coma, respiratory depression and cardiomyopathy. Ethanol has cross tolerance and shares similar behavioural problems with other CNS depressants including barbiturates and benzodiazepines.

Ethanol acutely decreases myocardial contractility and causes peripheral vasodilatation, resulting in hypotension and a compensatory increase in heart rate and cardiac output.

Ethanol is metabolised by alcohol dehydrogenase. In acute methanol and ethylene glycol poisoning, the parent compounds cause central nervous system depression, but acidosis, retinal damage (methanol) and renal failure (ethylene glycol) are caused by metabolites. These include formic acid (from methanol), glycolic acid, glyoxylic acid, and oxalic acid (from ethylene glycol). Breakdown of the parent compound by alcohol dehydrogenase is the first step in the formation of these toxic metabolites. This step is inhibited by ethanol, since alcohol dehydrogenase has a greater affinity for ethanol than it does for methanol or ethylene glycol. Methanol and ethylene glycol are then slowly metabolised to non-toxic compounds by alternative pathways, or may be removed by haemodialysis.

Direct application of ethanol to nervous tissue results in destruction of nerve fibres and cell bodies.

Pharmacokinetics

Ethanol is rapidly distributed throughout body fluids, with a volume of distribution of approximately 0.6 L/kg. It readily crosses the placenta. 90 to 98% of ethanol is metabolised in the liver. The majority of this is metabolised via alcohol dehydrogenase to acetaldehyde, which is further metabolised by aldehyde dehydrogenase to acetic acid. A second pathway, which operates optimally at higher ethanol concentrations, oxidises ethanol via a microsomal oxidising system, which is induced by repeated exposure to ethanol. The remaining 2% to 10% of ethanol is excreted directly via the kidneys, lungs, sweat or other bodily secretions. Ethanol is also excreted in breast milk.

Indications

Dehydrated Alcohol BP is indicated as an adjunct in the treatment of acute methanol and ethylene glycol poisoning.

Dosage and administration

Dehydrated Alcohol BP should be used as an adjunct to other treatments for methanol and ethylene glycol poisoning. Particular consideration should be given to haemodialysis, which has been shown to rapidly reduce blood concentrations of methanol and ethylene glycol. Folate, pyridoxine and thiamine may also be indicated to support metabolism by alternate pathways.

Dehydrated Alcohol BP must be diluted before administration. It should be administered as an intravenous infusion, as a 10% solution diluted in 5% glucose in water for injections. Using aseptic technique, add 100 mL of Dehydrated Alcohol BP to 900 mL of 5% glucose in water for injection. This solution is hypertonic, but has been administered safely via a peripheral vein in clinical practice. Infusion pain or phlebitis may necessitate administration via a central venous catheter.

An infusion pump should be used to reduce fluctuations in the blood ethanol concentration.

The therapeutic range for blood ethanol concentrations in the treatment of methanol and ethylene glycol poisoning is 100 to 150 mg/dL (22 to 33 mmol/L; 0.1% to 0.15%; 0.1 to 0.15 g/dL). Dehydrated Alcohol BP should be administered at a rate to achieve and maintain this concentration (see Table). Patients should be monitored for respiratory depression, particularly during administration of the loading dose. Blood ethanol levels should be checked regularly (eg hourly), and the infusion rate adjusted to ensure adequate ethanol levels are maintained, particularly during haemodilaysis.

Early treatment reduces the likelihood of permanent damage due to toxic metabolites. Ethanol therapy should be continued until methanol or ethylene glycol is undetectable in the blood. Treatment should be initiated as soon as possible using clinical criteria (eg history, symptoms, signs, anion gap metabolic acidosis) rather than waiting for confirmatory methanol or ethylene glycol blood concentrations.

Preparation: Using aseptic technique, add 100 mL Dehydrated Alcohol to 900 mL 5% glucose in water for injections		
Recommended dosage	**Non-drinker**	**Chronic drinker**
*Loading dose**		
Amount of ethanol	600 mg/kg	600 mg/kg
Volume of prepared **10% solution**	7.6 mL/kg	7.6 mL/kg
Maintenance dose#		
Amount of ethanol	66 mg/kg/h	
Volume of prepared **10% solution**	0.83 mL/kg/h	**
Maintenance dose during haemodialysis#		
Amount of ethanol	169 mg/kg/h	257 mg/kg/h
Volume of prepared **10% solution**	2.13 mL/kg/h	3.25 mL/kg/h

** The loading dose may need to be reduced in patients who have recently consumed ethanol.*

*** The maintenance dose may require increases of 2 to 3 fold in people who are chronic drinkers. Blood ethanol levels should be measured regularly and infusion rates adjusted as appropriate.*

 # These infusion rates are a guideline only. Blood ethanol levels should be measured regularly (eg hourly) and the infusion rate adjusted accordingly.

Compatibilities

Dehydrated alcohol is reported to be chemically stable and compatible with 5% glucose solution and 0.9% sodium chloride solution.

Contraindications

None known.

Warnings and precautions

Ethanol has central nervous system (CNS) depressant effects at therapeutic doses. Ethanol administration may potentiate the CNS side effects of methanol and ethylene glycol toxicity. Cardiorespiratory depression may result. Patients receiving Dehydrated Alcohol BP should be managed in an Intensive Care setting, with close monitoring of neurological and cardiorespiratory function. Facilities for resuscitation and manual ventilation should be available. Respiratory arrest has been reported with the recommended dose of ethanol.

During treatment of acute methanol or ethylene glycol poisoning, blood ethanol concentration should be checked regularly, to ensure that adequate levels are maintained. Ethanol's unpredictable kinetics lead to difficulty in maintaining effective therapeutic blood ethanol concentrations, particularly during haemodialysis, while avoiding drunkenness or toxic levels.

Blood glucose levels should be monitored during prolonged administration of Dehydrated Alcohol BP, because of possible hypoglycaemia.

Pregnancy and Lactation

Ethanol readily crosses the placenta. A foetal alcohol syndrome has been identified in infants born to some mothers who have consumed large or moderate amounts of alcohol orally during pregnancy. The foetal alcohol syndrome consists of abnormalities in; craniofacial development, prenatal and antenatal growth deficiencies, central nervous system dysfunction and various other abnormalities. Dehydrated Alcohol BP is therefore not recommended for use in pregnant women. However, as methanol and ethylene glycol toxicity may be fatal, or may lead to permanent blindness (methanol) or kidney failure (ethylene glycol), the risk to the foetus should be weighed against the benefits of the treatment.

Breast feeding should be temporarily suspended during treatment with Dehydrated Alcohol BP. Ethanol is excreted in breast milk, and its safety in neonates has not been established. Methanol and ethylene glycol may also be excreted in breast milk. Since treatment lasts no more than a few days, consideration should be given to expressing and discarding breast milk to preserve lactation.

Effects on ability to drive and use machines

As with other CNS acting drugs, Dehydrated Alcohol may affect the ability to perform tasks that require judgement or motor and cognitive skills. Patients should therefore exercise caution before driving or using machinery.

Other

Use in patients with hepatic impairment

Dehydrated Alcohol BP should be used with caution in patients with hepatic impairment, since the metabolism of ethanol may be reduced in such patients. Where hepatic impairment is due to excessive alcohol intake, the metabolism of ethanol may be decreased, or it may be paradoxically increased due to the induction of hepatic alcohol dehydrogenase.

Use in Children

Safety in neonates and children has not been established. However, as methanol and ethanol glycol toxicity may be fatal, or may lead to permanent blindness (methanol) or kidney failure (ethylene glycol), the possible risk to the infant or child should be weighed against the potential benefits of the treatment.

Use in the elderly

Dehydrated Alcohol BP should be used with caution in elderly patients as they may be more susceptible to the adverse effects of ethanol, such as orthostatic hypotension and central nervous system depression.

Use in regular alcohol drinkers

Consumption of ethanol leads to the induction of hepatic alcohol dehydrogenase. In patients who regularly drink significant amounts of alcohol, metabolism is increased and a higher dose of Dehydrated Alcohol BP is recommended (see **DOSAGE AND ADMINISTRATION**). Eventually, the induction of alcohol dehydrogenase may be offset by liver damage (see **PRECAUTIONS - Use in patients with hepatic impairment**).

Adverse effects

More common reactions:

Cardiovascular system: hypotension
Central Nervous system: loss of judgement, emotional lability, muscle coordination, visual impairment, slurred speech, ataxia, lethargy, amnesia
Gastrointestinal system: nausea, vomiting
Other: hypoglycaemia, hypothermia

Less common reactions:

Cardiovascular system: hypertension, cardiovascular collapse

Central Nervous system: coma
Other: transient hypoparathyroidism
Respiratory system: respiratory depression, respiratory arrest

Interactions

The following drugs may interact pharmacokinetically with Dehydrated Alcohol BP:

Drugs metabolised by the cytochrome P450 system:

Dehydrated Alcohol BP may compete with other drugs metabolised by this enzyme system, potentially decreasing the clearance of both drugs. Chronic administration of Dehydrated Alcohol BP may induce the cytochrome P450 enzyme system, potentially increasing the clearance of drugs metabolised by this system when alcohol is not present.

Disulfuram:

Disulfuram interferes with ethanol metabolism at the aldehyde stage, leading to unpleasant or, at larger concentrations, dangerous increase in aldehyde concentrations. Similar interactions may occur with cephalosporins, chlorpropamide, metronidazole, and tolbutamide.

Oral contraceptives:

Women taking oral contraceptives may have decreased elimination of ethanol.

The following drugs may interact pharmacodynamically with Dehydrated Alcohol BP:

Central Nervous System depressants

(such as hypnotics, muscle relaxants, opioid analgesics, antiepileptics, antidepressants and tranquilisers): Dehydrated Alcohol BP may enhance the depressant effects of these drugs.
Insulin: Dehydrated Alcohol BP may cause hypoglycaemic reactions in patients receiving insulin.

Oral anticoagulants:

Dehydrated Alcohol BP may have variable effects on bleeding time in patients taking oral anticoagulants.

Sulphonylurea antidiabetic agents:

Dehydrated Alcohol BP may cause hypoglycaemic reactions in patients receiving these agents.

Vasodilators:

Dehydrated Alcohol BP may cause orthostatic hypotension in patients taking vasodilator agents or drugs with vasodilator action.

Vasopressin:

Dehydrated Alcohol BP may decrease the antidiuretic effect of vasopressin.

Overdosage

Clinical features

The symptoms of ethanol overdosage are mainly a result of its CNS depressant effects. Muscle incoordination, visual impairment, slurred speech, ataxia and lethargy may progress to coma, respiratory depression, and cardiovascular collapse. The median lethal blood alcohol concentration is estimated to be 400 to 500 mg/100 mL in adults, although death may occur at lower concentrations due to aspiration of vomit during unconsciousness or the concurrent presence of other CNS depressants. An ingested dose of approximately 14 mL/kg may be fatal in children.

Treatment

There is no specific antidote for acute alcohol overdose. Treatment of overdose is symptomatic and supportive. Treatment may involve the following measures:

- haemodialysis is of value in severe alcohol poisoning.
- support of respiratory and metabolic functions.
- gastric lavage should be undertaken for accidental oral ingestion.

Pharmaceutical precautions

Incompatibilities

Dehydrated Alcohol BP is reported to be incompatible with Hartmann's solution, plasma protein preparations and phenobarbitone.

Effects on laboratory tests

It has been reported that alcohol may interfere with tests for serum acid phosphatase and ionised calcium.

Special Precautions for Storage

Store below 25°C. Protect from light.

Medicine classification

Prescription Medicine.

Package quantities

Strength	Dosage Form	Packs
100% Ethanol	Injection, solution	1 X 20 mL vial

Further information

Dehydrated alcohol is miscible with water, chloroform, ether, glycerol, and almost all other organic solvents.

The molecular formula of ethanol is C_2H_5OH. Its molecular weight is 46.07. The CAS Registry number of ethanol is 64-17-5.

Name and address

Mayne Pharma Pty Ltd
P O Box 17055
Karori
Wellington

Date of preparation

1 July 2004