

ESPERAL

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Abbreviated Prescribing information for ESPERAL (Disulfiram 250 mg Tablet) [Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES: *Pharmacodynamic properties* the effect of Disulfiram is primarily due to irreversible inactivation of liver ALDH. In the absence of this enzyme, the metabolism of ethanol is blocked and the intracellular acetaldehyde concentration rises. The symptoms of the Disulfiram-alcohol reaction (DAR) are due partly to the high levels of acetaldehyde. The conversion of dopamine to noradrenaline is also inhibited and the depletion of noradrenaline in the heart and blood vessels allows acetaldehyde to act directly on these tissues to cause flushing, tachycardia and hypotension. In addition to its effect on acetaldehyde dehydrogenase, disulfiram inhibits other enzyme systems including dopamine-beta-hydroxylase (which converts dopamine and noradrenaline) and hepatic microsomal mixed function oxidases (which are responsible for the metabolism of many drugs). Disulfiram may thus potentiate the action of drugs which are metabolised by these enzymes. *Pharmacokinetic properties* Following oral administration, absorption is variable, distribution is primarily to the kidney, pancreas, liver, intestines and fat. Disulfiram is rapidly metabolised to diethyldithiocarbamic acid (DDC), is conjugated with glucuronic acid, oxidised to sulphate, methylated and decomposed to diethylamine and carbon disulphide. Excretion is primarily through the kidneys.

INDICATIONS: Alcohol deterrent compound. Disulfiram may be indicated as an adjuvant in the treatment of carefully selected and co-operative patients with drinking problems. Its use must be accompanied by appropriate supportive treatment.

DOSAGE AND ADMINISTRATION: As directed by physician. Dose should be taken orally

CONTRAINDICATION: Disulfiram is contraindicated in presence of cardiac failure, coronary artery disease, previous history of CVA, hypertension, severe personality disorder, suicidal risk or psychosis, consumption of alcohol, hypersensitivity to disulfiram or to any of the excipients.

WARNINGS & PRECAUTIONS: Caution should be exercised in the presence of renal failure, hepatic or respiratory disease, diabetes mellitus, hypothyroidism, cerebral damage and epilepsy. Alcohol must not be consumed during treatment and for up to 14 days after discontinuation, as disulfiram prevents the metabolism of ethanol, causing acetaldehyde to accumulate in the body. This can result in a “disulfiram-alcohol reaction” causing adverse effects. Before initiating treatment, it is advised that appropriate examinations should be carried out to establish the suitability of the patient for treatment. Patients must be warned of the unpredictable and potentially severe nature of a Disulfiram-alcohol reaction as, in rare cases deaths have been reported following the drinking of alcohol by patients receiving Disulfiram. Certain foods, liquid medicines, remedies, tonics, toiletries, perfumes and aerosol sprays may contain sufficient alcohol to elicit a Disulfiram-alcohol reaction and patients should be made aware of this. Caution should also be exercised with low alcohol and “non-alcohol” or “alcohol free” beers and wines, which may provoke a reaction when consumed in sufficient quantities. All personnel involved in the administration of Disulfiram to the patient know that Disulfiram should not be given during a drinking episode.

DRUG INTERACTIONS: Disulfiram blocks the metabolism of alcohol and leads to an accumulation of acetaldehyde in the blood stream. The intensity of the Disulfiram-alcohol reaction may be increased by amitriptyline. Chlorpromazine while decreasing certain components of the Disulfiram-alcohol reaction may increase the overall intensity of the reaction. Disulfiram inhibits the metabolism of certain benzodiazepines such as chlordiazepoxide and diazepam enhancing their sedative effect. The interaction is not indicated for oxazepam. Benzodiazepines may reduce the disulfiram-alcohol reaction. Disulfiram inhibits the metabolism of many drugs which are converted in the liver (such as phenytoin, theophylline

and warfarin) and thereby enhances efficacy. Dose adjustment may be necessary. Animal studies have indicated similar inhibition of metabolism of pethidine, morphine and amphetamines. A few case reports of increase in confusion and changes in affective behaviour have been noted with the concurrent administration of metronidazole, isoniazid or paraldehyde. Potentiation of organic brain syndrome and choreoathetosis following pimozide have occurred very rarely. Disulfiram inhibits the oxidation and renal excretion of rifampicin.

ADVERSE REACTIONS: *Psychiatric disorders:* psychotic reactions; depression, paranoia, schizophrenia, mania, reduction in libido, Nervous system disorders, drowsiness (during initial treatment), peripheral neuritis, optic neuritis, encephalopathy, Gastrointestinal disorders, nausea, vomiting, Hepatobiliary disorders, hepatic cell damage, Skin and subcutaneous tissue disorders, allergic dermatitis, General disorders and administration site conditions, fatigue (during initial treatment), halitosis, *Disulfiram-alcohol reaction:* Disulfiram irreversibly inhibits acetaldehyde dehydrogenase. Intake of ethanol during disulfiram therapy will lead to accumulation of acetaldehyde, which is considered the main contributing factor to the disulfiram-alcohol reaction Disulfiram-ethanol reactions often develop within 15 minutes after exposure to ethanol; symptoms usually peak within 30 minutes to 1 hour, and then gradually subside over the next few hours. Symptoms may be severe and life-threatening. *The disulfiram- alcohol reaction is characterised by:* Intense vasodilation of the face and neck causing flushing, increased body temperature, sweating, nausea, vomiting, pruritis, urticaria, anxiety, dizziness, headache, blurred vision, dyspnoea, palpitations and hyperventilation, In severe cases tachycardia, hypotension, respiratory depression, chest pain, QT prolongation, ST depression, arrhythmias, coma and convulsions may occur. Rare complications include hypertension, bronchospasm and methaemoglobinaemia.

MARKETED BY:



TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

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(Additional information is available on request)