Proval CR

Sodium Valproate and Valproic Acid Controlled Release Tablet

Presentation

Proval CR 200 tablet: Each film coated controlled release tablet contains Sodium Valproate BP 133.2 mg & Valproic acid BP 58 mg (Both together correspond to sodium valproate 200 mg).
Proval CR 300 tablet: Each film coated controlled release tablet contains Sodium Valproate BP 199.8 mg & Valproic acid BP 87 mg (Both together correspond to sodium valproate 300 mg).
Proval CR 500 tablet: Each film coated controlled release tablet contains Sodium Valproate BP 333 mg & Valproic acid BP 145 mg (Both together correspond to sodium valproate 500 mg).

Description

Sodium Valproate, the active ingredient of Proval CR is endowed with anti-epileptic activity against a variety of seizures. The mechanism by which Sodium Valproate exerts its anti-epileptic effects has not been established. However, it has been suggested that its activity is related to increase brain levels of gamma-aminobutyric acid (GABA).

Indications

Proval CR is indicated for the treatment of all types of epilepsy, e.g. Partial seizures. Absence seizures (petit mal), Generalized tonic-clonic seizures (grand mal). Myoclonic seizures. Atonic seizures, Mixed seizures that include absence attack. Prophylaxis of febrile convulsion. Prophylaxis of post-traumatic epilepsy. It is also indicated in the treatment of bipolar disorder & prophylaxis of migraine.

Dosage and administration

Proval CR is a prolong release formulation of Sodium Valproate, thus Proval CR may be given once or twice daily.

Epilepsy - Adults	Initially 600 mg daily given in 2 divided doses, preferably after food, increasing by 200 mg/day at 3-day intervals to a maximum of 2.5 g daily in divided doses until control of seizure is achieved. Usual maintenance dose is 1-2 g daily (20-30 mg/kg daily).
Children (up to 20 kg)	Initially 20 mg/kg dally in divided doses, may be increased provided plasma concentrations monitored (above 40 mg/kg daily also monitor clinical chemistry and hematological parameters).
Children (Over 20 kg)	Initially 400 mg daily in divided doses increased until control (usually in the range of 20-30 mg/kg daily); Maximum 35 mg/kg daily
Febrile convulsion	20-30 mg/kg/day in 3 divided doses.
Bipolar disorder	Initially 20-30 mg/kg/day in 2-3 divided doses; adjust dosage in 3-5 days. Maintenance dosage is 1000-2000 mg-day.
Prophylaxis of migraine	300 mg twice daily, although some may require 1000 mg daily.

Use in Pregnancy & Lactation

Sodium Valproate crosses the placenta and in humans, exposure to valproate in the first trimester has been associated with neural tube defects such as anencephaly and spinabifida in newborn. Pregnant women treated with Proval CR should be offered to estimate serum a-fetoprotein. Proval CR is excreted in breastmilk. However, breast-feeding by a mother taking Proval CR probably causes no risk to the child.

Precautions

Liver functions should be monitored before therapy and during first 6 months especially in patients most at risk. No undue potential for bleeding before starting and before major surgery must be ensured, Care should be taken in renal impairment, pregnancy, breast-feeding and systemic lupus erythematosus. Sodium Valproate is partially eliminated in the urine as a ketone metabolite, which may lead to a talse interpretation of the urine ketone test. Sudden withdrawal of therapy should be avoided.

Contraindications

Sodium Valproate is contraindicated to patients who have known hypersensitivity to the drug and liver dysfunction. Care should be exercised when prescribing Sodium Valproate in women of child bearing age.

Overdose

Cases of accidental and deliberate Valproate overdosage have been reported. At plasma concentrations of up to 5 to 6 times the maximum therapeutic levels, there are unlikely to be any symptoms other than nausea, vomiting and dizziness. Signs of massive overdose, i.e. plasma concentration 10 to 20 time's maximum therapeutic levels, usually include CNS depression or coma with muscular hypotonia, hyporeflexia, miosis, impaired respiratory function, metabolic acidosis. A favorable outcome is usual; however some deaths have occurred following massive overdose. Symptoms may however be variable and seizures have been reported in the presence of very high plasma levels. Cases of intracranial hypertension related to cerebral oedema have been reported. Hospital management of overdose should be symptomatic, including cardio-respiratory monitoring. Gastric lavage may be useful up to 10 to 12 hours following ingestion. Haemodialysis and haemoperfusion have been used successfully. Naloxone has been successfully used in a few isolated cases, sometimes in association with activated charcoal given orally. In case of massive overdose, haemodialysis and haemoperfusion have been used successfully.

Drug Interactions

Sodium Valproate appears to act as a non-specific inhibitor of drug metabolism. Drugs to which it interacts most significantly are Phenobarbital. Phenytoin. Warfarin, Aspirin etc.

Side effects

The most common side effects are anorexia, nausea and vomiting However, these side effects are minimized with the use of enteric coated tablets. Effects on the CNS include sedation, ataxia and tremor. These symptoms occur infrequently and usually respond to a decrease in doses. Rash, alopecia and stimulation of appetite have been observed occasionally. Sodium Valproate has several effects on hepatic function of which elevation of liver enzymes in plasma is observed in up to 40% of patients and often occurs asymptomatically during the first few months of therapy. Rarely a fulminate hepatitis that may be fatal may develop. Children below 2 years of age with other medical conditions and those being treated with multiple antiepileptic agents are specially prone to suffer from hepatic injury, acute pancreatitis and hyperammonemia have also been frequently associated with the use of Sodium Valproate.

Storage conditions

Store in a cool and dry place, away from light. Keep out of the reach of children.

Commercial Pack

Proval CR 200 tablet: Each box contains 05 blister packs of 08 tablets.
Proval CR 300 tablet: Each box contains 05 blister packs of 08 tablets.
Proval CR 500 tablet: Each box contains 05 blister packs of 04 tablets

Manufactured by:
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