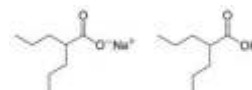


Rx VALPROATE SEMISODIUM

(vial contains 8.8 mg somatropin, 60.2 mg sucrose and 2.05 mg O-phosphoric acid)



Drug Class Description : Anti-manic agents

Generic Name : Valproic acid (as valproate semisodium)

Drug description : Containing 269.10mg of valproate semisodium* per tablet (equivalent to 250mg of valproic acid). Containing 538.20mg of valproate semisodium* per tablet (equivalent to 500mg of valproic acid). *Valproate semisodium is a stable coordination compound comprised of sodium valproate and valproic acid in a 1:1 molar relationship. It is also known as divalproex sodium (USAN).

Presentation : Gastro-resistant tablets.

Indications : Depakote is indicated for the acute treatment of a manic episode associated with bipolar disorder.

Adult Dosage :

For oral administration. The tablets should be swallowed whole with a drink of water, and not crushed or chewed.

The daily dosage should be established according to age and body weight. The wide variation in individual sensitivity to Depakote should also be considered.

There is no clear correlation between daily dose, plasma concentration and therapeutic effect. Optimum dosage should be determined mainly by clinical response. Measurement of valproate plasma levels may be considered in addition to clinical monitoring when adequate therapeutic effect is not achieved or adverse effects are suspected.

In mania it is generally agreed that plasma levels around 45 to 50µg/ml are needed to allow efficacy; most patients receiving Depakote during controlled clinical trials achieved a maximum plasma concentration of greater than 75µg/ml.

Dosage

Adults

The recommended initial dose is 750mg daily in 2 to 3 divided doses. From day 2 the dose should be increased as rapidly as possible to achieve the lowest therapeutic dose which produces the desired clinical effect. Daily doses usually range between 1000 and 2000mg (i.e. 20–30 mg/kg/day body weight). Where adequate control is not achieved within this range the dose may be increased.

Patients receiving daily doses higher than 45mg/kg/day body weight should be carefully monitored.

In patients with renal insufficiency

It may be necessary to decrease dosage. Dosage should be adjusted according to clinical monitoring since monitoring of plasma concentrations may be misleading.

In patients with hepatic insufficiency

Salicylates should not be used concomitantly with Depakote since they employ the same metabolic pathway

Liver dysfunction, including hepatic failure resulting in fatalities, has occurred in patients whose treatment included valproic acid.

Salicylates should not be used in children under 16 years (see aspirin/salicylate product information on Reye's syndrome). In addition in conjunction with Depakote, concomitant use in children under 3 years can increase the risk of liver toxicity.

Combined Therapy

When starting Depakote in patients, already on anticonvulsants, these should be tapered slowly; if clinically possible; initiation of Depakote therapy should then be gradual, with target dose being reached after about 2 weeks. Faster titration may be permissible if plasma level monitoring is available. In certain cases it may be necessary to raise the dose by 5 to 10mg/kg/day when used in combination with anticonvulsants which induce liver enzyme activity, e.g. phenytoin, phenobarbital and carbamazepine. Once known enzyme inducers have been withdrawn it may be possible to maintain control on a reduced dose of Depakote. When barbiturates are being administered concomitantly and particularly if sedation is observed the dosage of barbiturate should be reduced.

When using Depakote with other psychotropics, a reduced dose may be required.

Optimum dosage is mainly determined by control. However, a method for measurement of plasma levels is available and may be helpful where there is poor control or side effects are suspected.

Child Dosage :

The safety and effectiveness of Depakote for the treatment of manic episodes have not been studied in individuals below the age of 18 years.

Elderly Dosage :

Although the pharmacokinetics of Depakote are modified in the elderly, they have limited clinical significance and dosage should be determined on the basis of clinical response

Contra Indications :

Active liver disease

Personal or family history of severe hepatic dysfunction, drug related

Hypersensitivity to valproate semisodium or any other ingredient of the preparation.

Porphyria

Special Precautions :

To ensure the correct medication is prescribed for the patient's condition, care must be taken not to confuse Depakote with Epilim or sodium valproate. Patients with bipolar disorder and epilepsy are distinct populations. These differences are reflected in the patient information leaflets which clearly indicate specific indications for these differing medications.

Although there is no specific evidence of sudden recurrence of underlying symptoms following withdrawal of valproate, discontinuation should normally only be done under the supervision of a specialist in a gradual manner. This is due to the possibility of sudden alterations in plasma concentrations giving rise to a recurrence of symptoms. NICE has advised that generic switching of valproate preparations is not normally recommended due to the clinical implications of possible variations in plasma concentrations.

Special Warnings

Liver dysfunction:

Conditions of occurrence:

Severe liver damage, including hepatic failure sometimes resulting in fatalities, has been very rarely reported. Experience in epilepsy has indicated that patients most at risk are infants and in particular young children under the age of 3 and those with severe seizure disorders, organic brain disease, and (or) congenital metabolic or degenerative disease associated with mental retardation.

After the age of 3, the incidence of occurrence is significantly reduced and progressively decreases with age.

The concomitant use of salicylates should be avoided in children under 3 due to the risk of liver toxicity. Additionally, salicylates should not be used in children under 16 years (see aspirin/salicylate product information on Reye's syndrome).

In most cases, such liver damage occurred during the first 6 months of therapy, the period of maximum risk being 2-12 weeks.

Suggestive signs:

Clinical symptoms are essential for early diagnosis. In particular, the following conditions which may precede jaundice should be taken into consideration, especially in patients at risk (see above: 'Conditions of occurrence'):

- non specific symptoms, usually of sudden onset, such as asthenia, malaise, anorexia, lethargy, oedema and drowsiness, which are sometimes associated with repeated vomiting and abdominal pain.

Note : This product information is intended only for residents of the India. Taj Pharmaceuticals Limited, medicines help to treat and prevent a range of conditions—from the most common to the most challenging—for people around the world.

Taj DRUG
WORLD

Taj Group of Companies ^{INDIA}

Taj Pharmaceuticals Ltd.

Phone : General EPA BX : 91 - (0)22 - 26374592/92 91,
(0)22 - 26374592/93 91 - (0)22 - 30601000,
Fax : 91-(0)22-26341274

Revised November 2010