

## **SODIUM VALPROATE tab, solution,drops, amp,syrup:**

**Class:** Anticonvulsant, Antimanic Agent.

**Indications:** Oral, I.V.: Monotherapy and adjunctive therapy in the treatment of patients with complex partial seizures; monotherapy and adjunctive therapy of simple and complex absence seizures; adjunctive therapy in patients with multiple seizure types that include absence seizures  
Additional indications: Depakote, Depakote ER, Stavzor: Mania associated with bipolar disorder; migraine prophylaxis  
Refractory status epilepticus, diabetic neuropathy

**Available dosage form in the hospital:** TAB 200MG, 200MG/ML DROPS, 300MG/ML SOLUTION, 400MG/4ML AMP, 50MG/ML SYRUP, SODIUM VALPROATE 333MG+ VALPROIC ACID 145 MG TAB

### **Dosage:**

**-Seizures: Note:** Administer doses >250 mg/day in divided doses.

-Oral:

-Simple and complex absence seizure: Initial: 15 mg/kg/day; increase by 5-10 mg/kg/day at weekly intervals until therapeutic levels are achieved; maximum: 60 mg/kg/day.

-Complex partial seizure: Initial: 10-15 mg/kg/day; increase by 5-10 mg/kg/day at weekly intervals until therapeutic levels are achieved; maximum: 60 mg/kg/day.

**Note:** Regular release and delayed release formulations are usually given in 2-4 divided doses per day; extended release formulation (Depakote ER) is usually given once daily. Depakote ER is not recommended for use in children <10 years of age. In patients previously maintained on regular release valproic acid therapy (Depakene) who convert to delayed release valproate tablets or capsules (Depakote, Stavzor), the same daily dose and frequency as the regular release should be used; once therapy is stabilized, the frequency of Depakote or Stavzor may be adjusted to 2-3 times daily.

**-Conversion to Depakote ER from a stable dose of Depakote:** May require an increase in the total daily dose between 8% and 20% to maintain similar serum concentrations.

**-Conversion to monotherapy from adjunctive therapy:** The concomitant antiepileptic drug (AED) can be decreased by ~25% every 2 weeks; dosage reduction of the concomitant AED may begin when valproate therapy is initiated or 1-2 weeks following valproate initiation.

**-I.V.:** Total daily I.V. dose should be equivalent to the total daily dose of the oral valproate product; administer dose as a 60-minute infusion ( $\leq 20$  mg/minute) with the same frequency as oral products; switch patient to oral products as soon as possible. Alternatively, rapid infusions of 1.5-6 mg/kg/minute have been used in clinical trials to quickly achieve therapeutic concentrations, and were generally well tolerated (Ramsay, 2003; Wheless, 2004; Venkataraman, 1999). One study reported undiluted valproic acid administered at  $\leq 10$  mg/kg/minute (dose of  $\leq 30$  mg/kg) was well tolerated (Limdi, 2007).

**-Status epilepticus, refractory (unlabeled use):** I.V.: Loading dose: 15-20 mg/kg administered at 20 mg/minute; maintenance dose: I.V. infusion: 1-5 mg/kg/hour (Gaitanis, 2003). Alternatively, median loading doses of 25-30 mg/kg (maximum dose: 45 mg/kg) administered at  $\leq 6$  mg/kg/minute have also been reported (Limdi, 2005; Misra, 2006; Sinha, 2000).

**-Mania: Oral:**

-*Depakote tablet, Stavzor*: Initial: 750 mg/day in divided doses; dose should be adjusted as rapidly as possible to desired clinical effect; maximum recommended dosage: 60 mg/kg/day

-*Depakote ER*: Initial: 25 mg/kg/day given once daily; dose should be adjusted as rapidly as possible to desired clinical effect; maximum recommended dose: 60 mg/kg/day.

**-Migraine prophylaxis: Oral:**

-*Depakote tablet, Stavzor*: 250 mg twice daily; adjust dose based on patient response, up to 1000 mg/day

-*Depakote ER*: 500 mg once daily for 7 days, then increase to 1000 mg once daily; adjust dose based on patient response; usual dosage range 500-1000 mg/day

**-Diabetic neuropathy (unlabeled use): Oral:** 500-1200 mg/day (Bril, 2011).

**Geriatric:**

Oral, I.V.: Lower initial doses are recommended due to decreased elimination and increased incidences of somnolence in the elderly; no specific dosage recommendations are provided by the manufacturer.

Upward titration should be done slowly and with close monitoring for adverse events (eg, sedation, dehydration, decreased nutritional intake). Safety and efficacy for use in patients >65 years have not been studied for migraine prophylaxis.

**Renal Impairment:**

-Mild-to-severe impairment: No dosage adjustment necessary; however, due to decreased protein binding in renal impairment, monitoring only total valproate concentrations may be misleading.

**Hepatic Impairment:**

-Mild-to-moderate impairment: Not recommended for use in hepatic disease; clearance is decreased with liver impairment. Hepatic disease is also associated with decreased albumin concentrations and 2- to 2.6-fold increase in the unbound fraction. Free concentrations of valproate may be elevated while total concentrations appear normal, therefore, monitoring only total valproate concentrations may be misleading.

-Severe impairment: Use is contraindicated

**Common side effect:**

Central nervous system: Headache ( $\leq 31\%$ ), somnolence ( $\leq 30\%$ ), dizziness (12% to 25%), insomnia (>1% to 15%), nervousness (>1% to 11%), pain (1% to 11%)

Dermatologic: Alopecia (>1% to 24%)

Gastrointestinal: Nausea (15% to 48%), vomiting (7% to 27%), diarrhea (7% to 23%), abdominal pain (7% to 23%), dyspepsia (7% to 23%), anorexia (>1% to 12%)

Hematologic: Thrombocytopenia (1% to 24%; dose related)

Neuromuscular & skeletal: Tremor ( $\leq 57\%$ ), weakness (6% to 27%)

Ocular: Diplopia (>1% to 16%), amblyopia/blurred vision ( $\leq 12\%$ )

Miscellaneous: Infection ( $\leq 20\%$ ), flu-like syndrome (12%)

**Pregnancy Risk Factor:** X (migraine prophylaxis)/D (all other indications)