VALPROSIM TABLETS

Divalproex Sodium 250 mg & 500 mg
Pack size: 10 x 10 tablets

DOSAGE AND ADMINISTRATION

Important: The following regimens refer to **delayed-release** divalproex tablets. Confirm whether Valprosim is delayed-release or extended-release before use; these formulations have different schedules and are not directly interchangeable.
Mania: Initial 750 mg/day in divided doses; adjust to clinical response and plasma concentrations.
Complex partial seizures: Start 10–15 mg/kg/day, increase by 5–10 mg/kg/day at weekly intervals.
Absence seizures: Start 15 mg/kg/day; increase by 5–10 mg/kg/day weekly.
Migraine prevention: Start 250 mg twice daily; adjust as prescribed, up to 1000 mg/day. Maximum recommended dose for seizure/mania regimens: 60 mg/kg/day.

DRUG INTERACTIONS

Carbapenem antibiotics can markedly lower valproate levels and should generally be avoided. Lamotrigine exposure increases, raising serious rash risk. Aspirin, warfarin and other anticoagulants may increase bleeding risk. Topiramate may increase risk of hyperammonemia or hypothermia. Enzyme-inducing antiseizure drugs and other agents can alter valproate concentrations. Monitor with concomitant medications.

PRESENTATION

Valprosim Tablets 250 mg: 10 x 10 tablets.
Valprosim Tablets 500 mg: 10 x 10 tablets.

COMPOSITION

Each 250 mg tablet contains divalproex sodium equivalent to 250 mg valproic acid. Each 500 mg tablet contains divalproex sodium equivalent to 500 mg valproic acid. Other ingredients are according to the approved product formula.

METHOD OF ADMINISTRATION

Swallow tablets whole; do not crush or chew. Take consistently as directed. Do not abruptly discontinue treatment for epilepsy because this may precipitate serious seizures. Dose changes and switching formulations require medical supervision.

PREGNANCY AND REPRODUCTIVE RISK

Avoid valproate in pregnancy and in patients who could become pregnant whenever effective alternatives exist. For epilepsy or bipolar disorder, use in pregnancy or in women of childbearing potential only when alternatives have failed or are unacceptable. Effective contraception and specialist counselling are essential. Do not stop seizure medicine without urgent prescriber advice.

SPECIAL POPULATIONS

Children under two years are at particularly high risk of fatal liver toxicity. In older patients, start cautiously, titrate slowly and monitor sedation, hydration and food intake. Use is contraindicated in significant hepatic dysfunction. Specialist monitoring may be needed in renal impairment or altered protein binding.

MANUFACTURED BY

Vega Pharmaceuticals (Pvt.) Ltd.

THERAPEUTIC CLASS

Antiepileptic / anticonvulsant; mood stabilizer; migraine prophylactic agent.

INDICATIONS

For approved delayed-release divalproex products: treatment of manic episodes associated with bipolar disorder; monotherapy or adjunctive therapy for specified seizure disorders, including complex partial and absence seizures; and prevention of migraine headaches in appropriate patients. Not indicated for treatment of an acute migraine attack.

CONTRAINDICATIONS

Hepatic disease or significant hepatic dysfunction; known POLG-related mitochondrial disorder or suspected POLG disorder in children under two years; known urea-cycle disorder; hypersensitivity to divalproex, valproate or ingredients. For migraine prophylaxis, contraindicated in pregnancy and in women of childbearing potential not using effective contraception.

ADVERSE REACTIONS

Nausea, vomiting, abdominal discomfort, tremor, somnolence, dizziness, headache, weight gain, hair loss and thrombocytopenia may occur. Serious reactions include hepatic injury, pancreatitis, hyperammonemic encephalopathy, severe skin reactions, bleeding disorders and suicidal ideation.

STORAGE

Store under the conditions approved for Valprosim, in the original packaging, protected from moisture. Keep out of reach of children. Do not use after expiry.

PHARMACOLOGY

Divalproex sodium dissociates to valproate in the gastrointestinal tract. Its antiseizure action is believed to involve increased brain gamma-aminobutyric acid (GABA) activity and effects on neuronal excitability.

BOXED WARNINGS — LIFE-THREATENING RISKS

HEPATOTOXICITY: Fatal hepatic failure has occurred, usually in the first six months. Risk is greater in children younger than 2 years and in mitochondrial disorders. Obtain liver tests before treatment and monitor frequently.
FETAL HARM: Exposure in pregnancy may cause neural tube defects, other malformations, reduced IQ and neurodevelopmental disorders.
PANCREATITIS: Life-threatening, sometimes fatal pancreatitis can occur. Severe abdominal pain, nausea or vomiting require urgent evaluation.

WARNINGS AND PRECAUTIONS

Monitor for unexplained lethargy, vomiting or mental-status change (possible hyperammonemia), unusual bruising or bleeding (thrombocytopenia), severe rash or systemic hypersensitivity, suicidal thoughts, hypothermia and marked sedation. Consider baseline and periodic blood counts/platelets and liver tests. Measure ammonia if encephalopathy is suspected.

OVERDOSAGE

May cause profound somnolence, heart block, hypotension, respiratory depression, metabolic abnormalities or coma. Seek emergency care immediately. Management is supportive; hospital treatment may include specific measures as clinically indicated.