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

Abridged Prescribing Information
VALPARIN ® CHRONO / ALKALETS / SYRUP
COMPOSITION :
Sodium Valproate Tablets I.P.
VALPARIN® 200 ALKALETS – Each enteric coated tablet contains Sodium Valproate I.P. 200mg
VALPARIN® 500 ALKALETS – Each enteric coated tablet contains Sodium Valproate I.P. 500mg
Controlled Release Tablets of Sodium Valproate and Valproic Acid
VALPARIN® CHRONO 200 - Sodium Valproate I.P. 133mg + Valproic Acid I.P. 58mg
VALPARIN® CHRONO 300 - Sodium Valproate I.P. 200mg + Valproic Acid I.P. 87mg
VALPARIN® CHRONO 500 - Sodium Valproate I.P. 333mg + Valproic Acid I.P. 145mg
Sodium Valproate Oral Solution I.P.
VALPARIN® 200 – Sodium Valproate I.P. 200mg/5ml
THERAPEUTIC INDICATIONS: (1) treatment of generalized or partial epilepsy, particularly with the following patterns of seizures : absence, myoclonic, tonic-clonic, atonic, mixed, as well as for partial epilepsy : simple or complex seizures, secondary generalized seizures, specific syndromes (West, Lennox-Gastaut). (2) treatment of manic episodes associated with bipolar disorders.
DOSAGE AND ADMINISTRATION : *For seizure control* : Initial daily dosage 10-15mg/kg, then titrated up to 20-30mg/kg. Careful monitoring required when receiving daily doses higher than 50mg/kg. Valparin Chrono allows once daily dosing. *For treating mania* Initially dosage 600mg daily increasing by 200mg/day at three-day intervals (Range : 1000 to 2000mg /day). When control is not achieved dose may be further increased to 2500mg/day.*Use in Children*: Epilepsy indication - Oral solution is more appropriate for children less than 11 years.Only for Bipolar indication – In children and adolescents the efficacy of valparin for the treatment of manic episodes in bipolar disorder has not beenestablished in patients aged less than18 years. Valproate treatment must be started and supervised by a doctor experienced in managing epilepsy or bipolar disorder.
SAFETY-RELATED INFORMATION: Contraindications: For treatment of epilepsy and biploar disorder contraindicated in pregnancy unless there is no suitable alternative treatment , in women of childbearing potential, unless the conditions of the pregnancy prevention program are fulfilled. For all indications:Hypersensitivity to sodium valproate or valproic acid. Acute and chronic hepatitis; Patient or family history of severe hepatitis, especially drug related; Hepatic porphyria; Patients known to have mitochondrial disorders caused by mutations in the nuclear gene encoding mitochondrial enzyme polymerase γ and in children under two years of age who are suspected of having a POLG-related disorder; Patients with known urea cycle disorders.
Warnings: Valproate has a high teratogenic potential and children exposed *in utero* to valproate have a high risk for congenital malformations and neurodevelopmental disorders
Available data show an increased risk of major congenital malformations and neurodevelopmental disorders in both valproate monotherapy and polytherapy compared to the population not exposed to valproate.
Severe liver damage resulting sometimes in fatalities has exceptionally been reported, severe pancreatitis which may result in fatalities has been very rarely reported. Monitoring of signs and symptoms of ototoxicity is recommended
*Estrogen-containing products:*Valproate does not reduce efficacy of hormonal contraceptives: However, estrogen-containing products, including estrogen-containing hormonal contraceptives, may increase the clearance of valproate, which may result in decreased serum concentration of valproate and potentially decreased valproate efficacy. Prescribers should monitor clinical response (seizure control or mood control) when initiating, or discontinuing estrogen-containing products. Consider monitoring of valproate serum levels.

Suicidal ideation and behavior : Patients should be monitored for signs of suicidal ideation and behavior and appropriate treatment should be considered.
Carbapenem agents : Concomitant use of valproate and carbapenem agents is not recommended.
Patients with known or suspected mitochondrial disease : Valproate may trigger or worsen clinical signs of underlying mitochondrial diseases caused by mutations or mitochondrial DNA as well as the nuclear-encoded POLG gene.
Aggravated convulsions
As with other antiepileptic drugs, some patients may experience, instead of an improvement, a reversible worsening of convulsion frequency and severity (including status epilepticus), or the onset of new types of

convulsions with valproate. In case of aggravated convulsions, the patients should be advised to consult their physician immediately.

Metamizole: Metamizole may decrease valproate serum levels when co-administered, which may result in potentially decreased valproate clinical efficacy. Prescribers should monitor clinical response (seizure control or mood control) and consider monitoring valproate serum levels as appropriate

Precautions: Liver function tests should be carried out before therapy, and periodically during the first 6 months especially in patients at risk. Blood tests are recommended prior to initiation of therapy or before surgery, and in case of spontaneous bruising or bleeding. Potential benefit should be weighed against its potential risk in patients with systemic lupus erythematosus. When a urea cycle enzymatic deficiency is suspected, metabolic investigations should be performed prior to treatment because of the risk of hyperammonemia with valproate. Patients should be warned of the risk of weight gain at initiation and appropriate strategies should be adopted to minimize the risk. Patients with an underlying carnitine palmitoyltransferase (CPT) type II deficiency should be warned of the greater risk of rhabdomyolysis when taking valproate. Alcohol intake is not recommended during treatment. Monotherapy is recommended in children under the age of 3 years. Concomitant use of salicylates should be avoided in children under 3 years of age due to the risk of liver toxicity. Appropriate liver monitoring should be exercised when valproate is used concomitantly with other anticonvulsants with potential hepatotoxicity, including cannabidiol, and dose reductions or discontinuation should be considered in case of significant anomalies of liver parameters.Patients with renal insufficiency should be closely monitored, it may be necessary to decrease the dosage.

Pregnancy : Valproate is contraindicated as treatment for bipolar disorder during pregnancy. Valproate is contraindicated as treatment for epilepsy during pregnancy unless there is no suitable alternative to treat epilepsy. Valproate is contraindicated for use in women of childbearing potential unless the conditions of the pregnancy prevention program are fulfilled

Neurodevelopmental disorders : Data have shown that exposure to valproate *in utero* can have adverse effects on mental and physical development of the exposed children. The risk of neurodevelopmental disorders (including that of autism) seems to be dose-dependent when valproate is used in monotherapy but a threshold dose below which no risk exists, cannot be established based on available data. When valproate is administered in polytherapy with other anti-epileptic drugs during pregnancy, the risks of neurodevelopment disorders in the offspring were also significantly increased as compared with those in children from general population or born to untreated epileptic mothers.Lactation : Excretion of valproate in breast milk is low with a concentration of 1% to 10% of maternal serum levels. Based on literature breastfeeding can be envisaged taking into account the valproate safety profile especially hematological disorders**.**

Adverse Reactions: Very common (≥10%): tremor, nausea, Common (≥1% and<10%) : anaemia, thrombocytopenia, extrapyramidal disorder, stupor, somnolence, convulsion, memory impairment, headache, nystagmus, dizziness, deafness, vomiting, gingival disorder (mainly gingival hyperplasia), stomatitis, abdominal pain upper, diarrhea, urinary incontinence, hypersensitivity, transient and /or dose related alopecia, nail and nail bed disorders, hyponatraemia, weight increased, haemorrhage, liver injury, dysmenorrhea, confusional state, hallucinations, aggression, agitation, disturbance in attention. *Pediatric population-* There is a particular risk of severe liver damage in infants and young children especially under the age of 3 years of age. Young children are also at particular risk of pancreatitis. These risks decrease with increasing age. Psychiatric disorders such as abnormal behavior, psychomotor hyperactivity and learning disorder are principally observed in the pediatric population

For full prescribing information, please contact Sanofi Healthcare India Private Limited, Sanofi House, CT Survey No 117-B, L& T Business Park, Saki Vihar Road, Powai, Mumbai-400072
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