Summary of prescribing information for DIVAA OD tablets

Active Ingredient: each extended-release tablet of DIVAA OD contains: divalproex sodium eq. to valproic acid 250mg, 500mg, 750mg, 1gm. **Indication:** As monotherapy or adjunctive therapy in the treatment of patients with complex partial seizure and manic episodes associated with bipolar disorder. For prophylaxis of migraine headache in adults with warning for pregnant women. **Dosage:** intended for once-a-day oral administration; should be swallowed whole and should not be crushed or chewed. Epilepsy: Start at 10 to 15 mg/kg/day, increasing at 1 week intervals by 5 to 10 mg/kg/day to achieve optimal clinical response; if response is not satisfactory, check valproate plasma level; maximum 60 mg/kg/day. Mania: Mania: Initial dose is 750 mg daily, increasing as rapidly as possible to achieve therapeutic response or desired plasma level. The maximum recommended dosage is 60 mg/kg/day. Migraine: starting dose 500 mg once daily for 1 week, thereafter increasing to 1000 mg once daily. Effective dose range: 500-1000 mg/day. Conversion from enteric-coated divalproex tablets to DIVAA OD: should be administered once-daily using a dose 8 to 20% higher than the total daily dose of enteric-coated divalproex tablets. **Contraindications:** Hepatic disease or significant hepatic dysfunction, Known mitochondrial disorders caused by mutations in mitochondrial DNA polymerase γ (POLG), Suspected POLG-related disorder in children under two years of age, Known hypersensitivity to the drug, Urea cycle disorders, Prophylaxis of migraine headaches: Pregnant women, women of childbearing potential not using effective contraception. **Warning and precautions:** Hepatotoxicity; evaluate high risk populations and monitor serum liver tests Birth defects, decreased IQ, and neurodevelopmental disorders following in utero exposure; should not be used to treat women with epilepsy or bipolar disorder who are pregnant or who plan to become pregnant or to treat a woman of childbearing potential unless other medications have failed to provide adequate symptom control or are otherwise unacceptable. Pancreatitis; divalproex should ordinarily be discontinued. Suicidal behavior or ideation; Antiepileptic drugs, including divalproex, increase the risk of suicidal thoughts or behaviour. Bleeding and other hematopoietic disorders; monitor platelet counts and coagulation tests. Hyperammonemia and hyperammonemic encephalopathy; measure ammonia level if unexplained lethargy and vomiting or changes in mental status, and also with concomitant topiramate use; consider discontinuation of valproate therapy. Hypothermia; Hypothermia has been reported during valproate therapy with or without associated hyperammonemia. This adverse reaction can also occur in patients using concomitant topiramate. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multiorgan hypersensitivity reaction; discontinue divalproex. Somnolence in the elderly can occur. Divalproex dosage should be increased slowly and with regular monitoring for fluid and nutritional intake. **Pregnancy & Lactation:** Pregnancy: can cause congenital malformations including neural tube defects, decreased IQ, and neurodevelopmental disorders. Lactation: Valproate is excreted in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for divalproex and any potential adverse effects on the breastfed infant from divalproex or from the underlying maternal condition. Monitor the breastfed infant for signs of liver damage including jaundice and unusual bruising or bleeding. **Interaction:** Hepatic enzyme-inducing drugs (e.g., phenytoin, carbamazepine, phenobarbital, primidone, rifampin) can increase valproate clearance, while enzyme inhibitors (e.g., felbamate) can decrease valproate clearance. Aspirin, carbapenem antibiotics, estrogen-containing hormonal contraceptives: Monitoring of valproate concentrations. Co-administration of valproate can affect the pharmacokinetics of other drugs (e.g. diazepam, ethosuximide, lamotrigine, phenytoin) by inhibiting their metabolism or protein binding displacement. Patients stabilized on rufinamide should begin valproate therapy at a low dose, and titrate to clinically effective dose. Dosage adjustment of amitriptyline/nortriptyline, propofol, warfarin, and zidovudine may be necessary if used concomitantly with divalproex. Topiramate: Hyperammonemia and encephalopathy. **Adverse reactions:** Most common abdominal pain, accidental injury, alopecia, amblyopia/blurred vision, amnesia, anorexia, asthenia, ataxia, back pain, bronchitis, constipation, depression, diarrhea, diplopia, dizziness, dyspepsia, dyspnea, ecchymosis, emotional lability, fever, flu syndrome, headache, increased appetite, infection, insomnia, nausea, nervousness, nystagmus, peripheral edema, pharyngitis, rash, rhinitis, somnolence, thinking abnormal, thrombocytopenia, tinnitus, tremor, vomiting, weight gain, weight loss. The safety and tolerability of valproate in pediatric patients were shown to be comparable to those in adults. **Overdose:** may result in somnolence, heart block, deep coma, and hypernatremia. Fatalities have been reported; patients have recovered from valproate levels as high as 2,120 mcg/mL. Management: hemodialysis or tandem hemodialysis plus hemoperfusion may result in significant removal of drug. The benefit of gastric lavage or emesis will vary with the time since ingestion. General supportive measures should be applied with particular attention to the maintenance of adequate urinary output. Naloxone has been reported to reverse the CNS depressant effects. Because naloxone could theoretically also reverse the antiepileptic effects of valproate, it should be used with caution.

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It is recommended to refer full prescribing information before prescription.

For further medical information, please write to: Intas Pharmaceuticals Ltd., Corporate House, Near Sola Bridge, SG highway, Thaltej, Ahmedabad-380054, Gujarat, India. productqueries@intaspharma.com