

The Carlat Psychiatry Report

DEPAKOTE (valproic acid) Fact Sheet

Manufacturer: Abbott, market exclusivity expires 2008; *Depakene* is available as a generic

Indications:

- Acute Mania (only Depakote *ER* is officially approved for this)
- Off-Label use for Prevention of Depression and Mania in Bipolar Disorder
- Off-label use for treating various problems related to impulsivity and rage

Mechanism: Unknown, may work by increasing GABA (gamma-aminobutyric acid)

Formulations:

- Depakene (comes in a 250 mg capsule or as a red syrup that contains 250 mg/5 mL): The brand name for valproic acid, which is the basic molecule of interest.
- Depakote (comes in non-scored, but breakable, tablets of 125 mg, 250 mg, and 500 mg): Brand name for “sodium divalproex”, which is two valproic acid molecules held together by sodium hydroxide. The “kote” in Depakote refers to the fact that it is packaged in an enteric-coated tablet.
- Depakote ER (comes in a very large 500 mg tablet): An extended release version of Depakote that is approved for once-daily dosing, but any of the versions of valproic acid can be dosed once-daily.
- Depakote Sprinkles (125 mg capsule that is easily opened for “sprinkling”): A good choice for patients who either hate swallowing pills or require an infinitesimally gradual dose titration because of side effects.

Dosing:

- Most clinicians dose Depakote at bedtime in order to increase compliance and minimize side effects, regardless of the formulation used.
- Start at 250-500 mg QHS, gradually increasing to achieve a blood Depakote level of 70-80 mcg/mL, which will often be in the 1000-1250 mg QHS range.
- When converting from regular Depakote to Depakote ER, be aware that patients will see about 20% less valproic acid with the ER formulation, making converting somewhat tricky, given that Depakote ER only comes in the 500 mg option.
- No dosing adjustment required in liver disease; if you dare to use it in a patient with chronic renal impairment, decrease the dose substantially, using the patient’s GFR as your guide.

Side Effects:

- Most common: nausea (switch to Depakote ER or Depakote sprinkles), fatigue, dizziness, tremor (treat with Inderal LA 60 mg QAM or regular Inderal 20 mg BID-TID)
- Thrombocytopenia (slight lowering of platelets not uncommon; significant problems more likely in elderly)
- Elevated liver function tests (not uncommon, usually benign, but need to monitor for very rare hepatic failure)
- Polycystic ovarian syndrome (PCOS) in about 10% of women (irregular periods, hirsutism, elevated testosterone)
- Black box warnings: Hepatotoxicity (rare, more likely to occur in young children), pancreatitis (also quite rare).
- Pregnancy Category D (high rate of neural tube defects)

Drug-drug interactions:

- Increases Lamictal levels; aspirin increases Depakote levels; combination with topiramate can lead to encephalopathy

Laboratory monitoring:

- Check Depakote level, CBC, LFTs after one week of treatment, at 1-2 months, then Q 6-12 months