DRUG NAME: DEPAKOTE, DEPAKOTE ER
Generic names: valproic acid, divalproex sodium, valproate

General Information: Depakote is an anticonvulsant drug approved for use in psychiatry to treat the manic phase of bipolar disorder. Though “off-label” and not officially approved by the FDA, it is also used for long-term stabilization of mood in bipolar disorder and to augment the effect of antidepressants in the treatment of severe depression and anxiety. The therapeutic mechanism of Depakote is not known, but may relate to increased concentration of GABA (gamma-aminobutyric acid) in the brain. GABA is an inhibitory neurotransmitter that slows firing rates in brain and muscle cells. Depakote is not habit-forming.

Guidelines for Use: Depakote is available in 125, 250, and 500 mg. tablets, and in “sprinkle” capsules that can be broken open and sprinkled on food (usually for children). Depakote ER (extended release) is available in 500 mg. tablets. Tablets should not be broken. No generic form is available at present. The usual starting dose of Depakote is about 750 mg. daily in divided doses. The usual starting dose of Depakote ER is 500 mg. nightly. Doses may be increased over time until a therapeutic blood level is achieved and clinical benefits are apparent. Improvement may be evident in 7-10 days, but it can take several more weeks to reach maximum benefit. Maintenance dosage in usually in the range of 1000-1500 mg. daily, sometimes higher. The target blood level is 50-100 micrograms/milliliter of blood, though some people’s symptoms are best controlled at slightly lower or higher levels. This drug may be taken with or without food.

If you forget to take this medication but remember within a few hours, take it when you remember. Otherwise, wait until your next dose. Do not take double doses. Store the drug in a dry, tightly-closed, light-resistant container out of the reach of children.

Side Effects of Depakote and Depakote ER:

*Note: Most side effects taper off during treatment as you become used to the drug.

Common side effects (10% or more of users experience; notify your clinician if severe):

- nausea, vomiting, diarrhea*  --drowsiness, lethargy
- dizziness                --weakness

Less common side effects (less than 10% of users experience; notify if severe):

- weight gain or loss       --hair loss       --hand tremor
- headache                 --constipation     --confusion, psychosis
- depression               --yellow eyes or skin**
- unusual bruising or bleeding#

*Significant nausea, vomiting and diarrhea accompanied by loss of appetite and abdominal pain may be signs of pancreatitis, an acute condition associated with
Depakote. It is a rare but serious problem, and may occur at any time during treatment. STOP THE DEPAKOTE AND SEEK MEDICAL CARE AS SOON AS POSSIBLE IF THESE SYMPTOMS OCCUR. If they are severe, go to an emergency room.

**Liver toxicity is another known rare but serious side effect of Depakote. It usually occurs in the first six months of treatment. Early symptoms include feeling unwell, weakness, lethargy, facial swelling, loss of appetite, and vomiting. Yellowing of eyes and skin and dark urine are a later development. People taking multiple drugs, or who have a history of impaired liver function, heavy use of alcohol or illegal drugs, or exposure to liver-toxic chemicals, are most at risk. IT IS IMPERATIVE THAT YOU LET YOUR CLINICIAN KNOW IF ANY OF THESE RISK FACTORS APPLY TO YOU. Your clinician will likely order lab work to assess your liver status before or early in treatment and at periodic intervals during treatment. BE SURE TO FOLLOW YOUR CLINICIAN’S INSTRUCTIONS FOR USE OF THIS DRUG CAREFULLY, OBTAIN ANY LAB WORK ORDERED IN A TIMELY WAY, AND REPORT ANY OF THE SYMPTOMS OF LIVER TOXICITY LISTED ABOVE.

#Depakote can reduce the count of platelets (clotting cells) in the blood, resulting in easy bruising or bleeding, particularly at higher doses. Report unusual bruising or bleeding to your clinician. Lab work to assess clotting status is part of routine monitoring with Depakote, and is also likely to be done prior to surgery or other procedure in which bleeding is a risk.

**Precautions:** Do not take this drug if you have ever had an allergic reaction to Depakote. Inform your clinician if you have any known drug allergies; if you have ever had seizures or been diagnosed with epilepsy, a bleeding disorder, pancreatitis, or liver disease; if you are taking any other drug (prescription or non-prescription), vitamin, supplement, or herb; if you have a history of heavy use of alcohol or illegal drugs; if you are undergoing anesthesia or surgery while taking this drug. **Inform your clinician if you are or might become pregnant.** Depakote is known to cause fetal abnormalities including spina bifida; it should not be taken by pregnant women or nursing mothers. Depakote should not be taken by children younger than 2 and should be used with great caution in older children. Metabolism of the drug may be slowed in the elderly; lower doses may be used.

**This drug often causes drowsiness, especially early in treatment.** If so, avoid driving or operating machinery until you are sure your coordination and alertness allow for safe operation.

Do not discontinue this drug without consulting with your clinician. You should be closely monitored for the re-emergence of symptoms when Depakote is stopped.

Overdoses of Depakote can result in sedation and coma; some fatalities have been reported. **SEEK IMMEDIATE EMERGENCY MEDICAL CARE IN CASES OF OVERDOSE, PARTICULARLY IF MULTIPLE DRUGS AND/OR ALCOHOL ARE SUSPECTED.**
**Interactions:**

**Alcohol:** You should avoid alcohol while using Depakote.

**Food/beverages:** No restrictions.

**Other drugs:** Below are listed drugs that interact with Depakote in important ways that might require dosage adjustments of one or both drugs. Discuss with your clinician.

Depakote INCREASES the blood levels of the following drugs: amitriptyline (Elavil, others), carbamazepine (Tegretol), clonazepam (Klonopin), diazepam (Valium), ethosuximide (Zarontin), lamotrigine (Lamictal), nortriptyline (Pamelor, others), phenobarbital (Luminal), Primidone (Mysoline), tolbutamide (Orinase), warfarin (Coumadin).

Depakote DECREASES the blood levels of these drugs: desipramine (Norpramin), phenytoin (Dilantin).

These drugs INCREASE THE BLOOD LEVEL OF DEPAKOTE: amitriptyline (Elavil, others), aspirin (Tylenol is OK), felbamate (Felbatol).

These drugs DECREASE THE BLOOD LEVEL OF DEPAKOTE: carbamazepine (Tegretol), Phenobarbital (Luminal), phenytoin (Dilantin), rifampin (Rifadin).

Depakote may increase the effects of other sedating medications such as antihistamines, sedatives, narcotic pain medicines, muscle relaxants, barbiturates, and anesthetics. Check with your clinician before taking these medications.