



College of Psychiatric and Neurologic Pharmacists (cpnp.org)

Valproate (val PROE ate)**Divalproex sodium** (dye val PRO ex)**Valproic acid** (val PROE ik AS id)

- **Depakene[®]**
 - Capsules (immediate release): 250 mg
 - Oral solution: 250 mg/mL
- **Depakote[®]**
 - Tablets (delayed release): 125 mg, 250 mg, 500 mg
 - Sprinkle capsules (delayed release): 125 mg
- **Depakote[®] ER**
 - Tablets (extended release): 250 mg, 500 mg
- **Stavzor[®]**
 - Capsules (delayed release): 125 mg, 250 mg, 500 mg

If you or someone you know is in crisis, please call 911 and/or the toll-free National Suicide Prevention Lifeline at 800-273-TALK (8255) to speak with a trained crisis counselor 24/7. A help line and other resources are also available through the National Alliance on Mental Illness at nami.org.



Note: For the purpose of this document, the medication will be referred to as valproate. Even though valproate is available in different names, strengths, and formulations, all provide the same active medicine.

What is valproate and what does it treat?

Valproate is a mood stabilizer medication that works in the brain. It is approved for the treatment of mania associated with bipolar disorder (also known as manic depression), seizures (epilepsy), and migraine headaches. Bipolar disorder involves episodes of depression and/or mania.

Symptoms of depression include:

- Depressed mood – feeling sad, empty, or tearful
- Feeling worthless, guilty, hopeless, or helpless
- Loss of interest or pleasure in normal activities
- Sleep and eat more or less than usual (for most people it is less)
- Low energy, trouble concentrating, or thoughts of death (suicidal thinking)
- Psychomotor agitation ('nervous energy')
- Psychomotor retardation (feeling like you are moving in slow motion)

Symptoms of mania include:

- Feeling irritable or 'high'
- Having increased self esteem
- Feeling like you don't need to sleep
- Feeling the need to continue to talk
- Feeling like your thoughts are too quick (racing thoughts)
- Feeling distracted
- Getting involved in activities that are risky or could have bad consequences (e.g. excessive spending)

Valproate may also be helpful when prescribed "off-label" for diabetic peripheral neuropathy, postherpetic neuralgia, status epilepticus, and some conditions related to a traumatic brain injury (agitation, aggression, and seizure prevention). "Off-label" means that it hasn't been approved by the Food and Drug Administration for this condition. Your mental health provider should justify his or her thinking in recommending an "off-label" treatment. They should be clear about the limits of the research around that medication and if there are any other options.

All FDA warnings are at the end of this fact sheet. Please consult them before taking this medication.

What is the most important information I should know about valproate?

Bipolar disorder requires long-term treatment. Do not stop taking valproate, even when you feel better. Only your healthcare provider can determine the length of valproate treatment that is right for you. Missing doses of valproate may increase your risk for a relapse in your mood symptoms.

Do not stop taking valproate or change your dose without talking to your healthcare provider first.

In order for valproate to work properly, it should be taken every day as ordered by your healthcare provider.

Periodically, your healthcare provider may ask you to provide a blood sample to make sure the appropriate level of medication is in your body and to assess for side effects, such as changes in blood cell counts.

Are there specific concerns about valproate and pregnancy?

If you are planning on becoming pregnant, notify your healthcare provider so that he/she can best manage your medications. People living with bipolar disorder who wish to become pregnant face important decisions. It is important to discuss the risks and benefits of treatment with your doctor and caregivers.

Valproate has been associated with an increased risk of spinal cord defects (spina bifida). Bleeding, liver problems, decreased IQ scores, developmental delays, and other birth defects have also been reported. There may be precautions to decrease the risk of these effects. Discontinuing mood stabilizer medications during pregnancy has been associated with a significant increase in symptom relapse.

Regarding breast-feeding, caution is advised since valproate does pass into breast milk in small amounts.

What should I discuss with my healthcare provider before taking valproate?

- Symptoms of your condition that bother you the most
- If you have thoughts of suicide or harming yourself
- Medications you have taken in the past for your condition, whether they were effective or caused any adverse effects
- If you experience side effects from your medications, discuss them with your provider. Some side effects may pass with time, but others may require changes in the medication.
- Any other psychiatric or medical problems you have
- All other medications you are currently taking (including over the counter products, herbal and nutritional supplements) and any medication allergies you have
- Other non-medication treatment you are receiving, such as talk therapy or substance abuse treatment. Your provider can explain how these different treatments work with the medication.
- If you are pregnant, plan to become pregnant, or are breast-feeding
- If you drink alcohol or use illegal drugs

How should I take valproate?

Valproate is usually taken 1-3 times daily with or without food.

Typically patients begin at a low dose of medicine and the dose is increased slowly over several weeks.

The dose usually ranges from 1000 mg to 3500 mg or more. Only your healthcare provider can determine the correct dose for you, as sometimes the dose required is based on your weight.

Valproate tablets: Swallow whole. Do not crush, chew or split tablets.

Depakote Sprinkle® capsules: Swallow whole or sprinkle onto food, such as applesauce or pudding and eat immediately. Do not chew the sprinkle capsule or contents.

Valproate syrup: Measure with a dosing spoon or oral syringe that you can get from your pharmacy.

Use a calendar, pillbox, alarm clock, or cell phone alert to help you remember to take your medication. You may also ask a family member a friend to remind you or check in with you to be sure you are taking your medication.

What happens if I miss a dose of valproate?

If you miss a dose of valproate, take it as soon as you remember, unless it is closer to the time of your next dose. Discuss this with your healthcare provider. Do not double your dose or take more than what is prescribed.

What should I avoid while taking valproate?

Avoid drinking alcohol or using illegal drugs while you are taking valproate. They may decrease the benefits (e.g., worsen your condition) and increase adverse effects (e.g., sedation) of the medication.

What happens if I overdose with valproate?

If an overdose occurs call your doctor or 911. You may need urgent medical care. You may also contact the poison control center at 1-800-222-1222.

A specific treatment to reverse the effects of valproate does not exist.

What are the possible side effects of valproate?

Common side effects

- Nausea or vomiting
- Headache
- Drowsiness or dizziness
- Tremor
- Muscle weakness
- Insomnia
- Hair loss
- Weight gain
- Diarrhea or abdominal pain

Rare/Serious side effects

- Liver problems
- Low platelets. Platelets help the blood to clot. Bruising easier than normal is a symptom of low platelets
- Pancreatitis (inflammation of the pancreas). Symptoms of pancreatitis include severe stomach pain, nausea, vomiting, and not feeling hungry
- Increased ammonia levels. If this happens, you may get confused, disoriented, or have difficulty thinking.

Studies have found that individuals who take antiepileptic medications including valproate have suicidal thoughts or behaviors up to twice as often than individuals who take placebo (inactive medication). These thoughts or behaviors occurred in approximately 1 in 550 patients taking the antiepileptic class of medications. If you experience any thoughts or impulses to hurt yourself, you should contact your doctor immediately.

Are there any risks for taking valproate for long periods of time?

To date, there are no known problems associated with long term use of valproate. It is a safe and effective medication when used as directed.

It is important to note that some of the side effects listed above (particularly changes in platelets, liver or pancreas problems, and suicidal thoughts) may continue to occur or worsen if you continue taking the medication. It is important to follow up with your doctor for blood work and to contact your doctor immediately if you notice abdominal pain, sudden nausea or vomiting, or changes in mood or behavior.

What other medications may interact with valproate?

Combining valproate with topiramate (Topamax®) may increase ammonia levels in your blood. If this happens, you may get confused, disoriented, or have difficulty thinking.

The following medications may **increase** the level and effects of valproate:

- Aspirin (high doses to treat fever or pain)

The following medications may **decrease** the level and effect of valproate:

- Anticonvulsant medications such as phenytoin (Dilantin®), carbamazepine (Tegretol®/Carbatrol®/Equetro®), and phenobarbital
- Rifampin (Rifadin®)
- Certain antibiotics, such as ertapenem (Invanz®) or meropenem (Merrem®)

Valproate may **increase** the level and effects of:

- Antidepressant medications such as amitriptyline (Elavil®) and nortriptyline (Pamelor®)
- Anticonvulsant medications such as phenytoin (Dilantin®), carbamazepine (Tegretol®/Carbatrol®/Equetro®), rufinamide (Banzel®), ethosuxamide (Zarontin®), and especially lamotrigine (Lamictal®).
- Diazepam (Valium®)

Valproate may **decrease** the level and effects of:

- Olanzapine (Zyprexa®)
- Oxcarbazepine (Trileptal®)

How long does it take for valproate to work?

It is very important to tell your doctor how you feel things are going during the first few weeks after you start taking valproate. It will probably take several weeks to see big enough changes in your symptoms to decide if valproate is the right medication for you.

Mood stabilizer treatment is generally needed lifelong for persons with bipolar disorder. Your doctor can best discuss the duration of treatment you need based on your symptoms and illness.

Summary of Black Box Warnings

Liver Damage

Serious and fatal liver damage has been associated with valproate, particularly during the first six months of treatment. These risks are increased in patients that also have co-occurring mitochondrial disease.

Birth Defects

Birth defects have been found in babies born to mothers who took valproate while pregnant.

Pancreatitis

Life threatening pancreatitis has been reported in children and adults who take valproate. Signs of pancreatitis include severe abdominal pain, nausea, vomiting and inability to keep food down.

Important Disclosure: This information is being provided as a community outreach effort of the College of Psychiatric and Neurologic Pharmacists. This information is for educational and informational purposes only and is not medical advice. This information contains a summary of important points and is not an exhaustive review of information about the medication. Always seek the advice of a physician or other qualified medical professional with any questions you may have regarding medications or medical conditions. Never delay seeking professional medical advice or disregard medical professional advice as a result of any information provided herein. The College of Psychiatric and Neurologic Pharmacists disclaims any and all liability alleged as a result of the information provided herein.