

## Using *divalproex / valproic acid* (*Epival*<sup>®</sup> / *Depakene*<sup>®</sup>) in Children and Adolescents



### Overview

*Divalproex / valproic acid (Epival<sup>®</sup> / Depakene<sup>®</sup> and generic forms)* belong to a group of medications called “mood stabilizers”. Divalproex is converted to valproic acid in the body, and the two medications are very similar. Some patients may find that divalproex is easier on the stomach than valproic acid. Note: both medications are referred to as “**valproic acid**” in this document.

### What is *valproic acid* used for?

Valproic acid is approved by Health Canada to treat certain types of seizure disorders (epilepsy) in adults and children two years of age and older. This medication is sometimes called an “antiepileptic” or “anticonvulsant”. Valproic acid is also approved by Health Canada for the treatment of bipolar disorder in adults age 18 and over. When used this way, valproic acid is sometimes called a “mood stabilizer”. Like many other medications prescribed for children and adolescents, Health Canada has not approved valproic acid for management of bipolar disorder in this age group. When the potential benefits (e.g., reducing your symptoms) of using valproic acid outweigh the potential risks (e.g., the side effects), many doctors may prescribe it “off-label” to treat several conditions such as:

- Treatment of episodes of mania (elevated mood) or depression associated with bipolar disorder
- Prevention of future manic or depressive episodes associated with bipolar disorder
- Impulsive or aggressive behaviour
- Prevention of migraine headaches

Your doctor may be using this medication for another reason. If you are unclear why this medication is being prescribed, please ask your doctor.

### How does *valproic acid* work?



Valproic acid may affect the activity of certain brain chemicals (neurotransmitters) called GABA and glutamate. This medication has a “stabilizing” effect on nerves, which in turn helps to reduce severe mood fluctuations associated with bipolar disorder. The exact way valproic acid improves symptoms of bipolar disorder is still not fully known.

### How well does *valproic acid* work in children and adolescents?

There is evidence to show that valproic acid reduces symptoms of a manic or depressive episode associated with bipolar disorder in children and adolescents. It may also prevent future episodes of mania or depression from occurring. Valproic acid may be used alone or in combination with other mood stabilizers to manage bipolar disorder.

When treating a manic episode, valproic acid may improve symptoms such as: an elevated, expansive or irritable mood; a reduced need for sleep; fast/increased talking; an inflated self-esteem or feelings of grandiosity; being easily distracted; racing thoughts; high-risk behaviours; taking part in an excessive amount of activities.

When treating a depressive episode (usually along with other medication(s)), valproic acid may improve symptoms such as: prolonged sadness; decreased interest or pleasure; difficulty sleeping or sleeping too much; changes in appetite and weight; loss of energy or extreme tiredness; slowed movements or agitated behaviour; feelings of worthlessness, guilt or hopelessness; impaired concentration or decision-making skills; thoughts or attempts of suicide and self-harm.

When effective, valproic acid helps to stabilize your mood and return your activity level to normal. This medication may help you to have more control over your emotions and to improve your overall functioning. Valproic acid may be particularly helpful for patients who have symptoms of mania and depression occurring at the same time (a 'mixed' episode) or who have more than four mood episodes per year (this is called 'rapid cycling'). This medication may also specifically target aggressive or impulsive behavioural problems. Whenever possible, adding education about your condition (for example: teaching you how to recognize early warning signs of a manic episode and the appropriate coping strategies) increases the chance you will benefit from taking this medication.

### How should *valproic acid* be taken?



Valproic acid (Depakene<sup>®</sup> and generic forms) comes in regular capsules and as a syrup, both of which are taken by mouth. Divalproex (Epival<sup>®</sup> and generic forms) comes in enteric-coated tablets that are taken by mouth. Usually, both forms are taken two or three times daily. Valproic acid capsules and tablets should be swallowed whole, and should not be chewed. Doing so may irritate your mouth and throat. Valproic acid syrup may be mixed with food or liquids to help you take the medication. Take valproic acid with food to reduce the chance of stomach upset.

When starting treatment, your doctor may initially prescribe a low dose of valproic acid that is taken two or three times daily. Then, the dose may be gradually increased every 3 to 7 days. Your doctor will determine how much you should take, according to your weight, how much medication is in your body and your response to this medication. The blood level of valproic acid required to be effective varies, but for most people, the desired blood level is somewhere between 350-700 micromoles/L. Do not take your valproic acid dose just before having a blood test to check your blood level, as this can affect your blood level results. Instead, take your dose right after the blood test is completed.

Valproic acid needs to be taken regularly on a daily basis in order to be effective (even if you feel well). Valproic acid should be taken at the same times each day as directed by your doctor. Try connecting it with something you do at those times (for example: brushing your teeth) to help you remember the doses. Treatment with valproic acid should usually not be stopped suddenly, as it may lead to uncomfortable withdrawal effects. If you are taking valproic acid for a seizure disorder, stopping valproic acid suddenly may trigger seizures. Do not drink alcoholic beverages while taking valproic acid, as this may result in increased side effects.

### When will *valproic acid* start working?

When used as a mood stabilizer to control a manic episode, valproic acid needs to be taken for 1 to 2 weeks before you notice an improvement in your symptoms. You may notice an improvement earlier if valproic acid is combined with other medications. Unless directed by your doctor, do not increase, decrease, or stop taking the medication if there are no improvements in the first few weeks. A delay in response is normal. Valproic acid may not work for everyone. If you find this medication has not helped you after a month of treatment or the side effects are too bothersome, your doctor may recommend switching you to a different medication.

### How long do I have to take *valproic acid*?



This depends on the symptoms you have, how frequently they occur and how long you have had them. Most people who have bipolar disorder need to take valproic acid for at least 6 months. This allows your symptoms to stabilize and for you to regain functioning while decreasing your risk of another mood episode. After 6 months of treatment, you and your doctor can discuss the benefits and risks of continuing treatment.

If you have had several episodes of mania or depression and you tolerate this medication well, you may be asked to take this medication indefinitely. By continuing to take this medication, your risk of having another mood episode is significantly decreased. Even if you are feeling better, do not stop taking this medication suddenly without first discussing it with your doctor. After you have been taking valproic acid on a regular basis, stopping it suddenly may trigger uncomfortable withdrawal effects and increase your risk for having a seizure. If you and your doctor decide to stop using valproic acid, your doctor will explain how to safely lower the dose gradually.

## Is valproic acid addictive?

Valproic acid is not addictive. You will not have “cravings” for it like some people do with nicotine or street drugs.

## What are the side effects of valproic acid and what should I do if I get them?

As with most medications, side effects may occur when taking valproic acid. However, most side effects are mild and temporary. Sometimes the side effects may occur before any of the beneficial effects. It is also possible for some individuals to experience side effects that they feel are concerning or long-lasting. If this occurs, speak to your doctor about ways to manage them. Below are some of the more common side effects of taking this medication. In brackets are suggested ways to lessen these effects.

### Common side effects

Side effects are usually more common when starting a medication or after a dose increase. If any of these side effects is troublesome for you, please discuss them with your doctor, nurse or pharmacist.

- Clumsiness, unsteadiness, tiredness (*avoid activities that require physical coordination until you know how this medication affects you*)
- Drowsiness, clouded thinking, confusion (*avoid alcoholic drinks with this medication. Do not drive, operate machinery or participate in activities requiring mental alertness until you know how this medication affects you.*)
- Hair loss (*this may occur after 3 to 6 months of treatment and usually improves with time*)
- Headache (*try using a pain reliever like acetaminophen (Tylenol®)*)
- Restlessness (*try avoiding caffeinated beverages such as coffee, tea, or colas*)
- Shakiness (tremor) of the hands (*discuss with your doctor if it becomes bothersome or persistent; try avoiding caffeine from colas, coffee, or tea*)
- Stomach ache, nausea, vomiting, diarrhea (*try taking the medication with food. Divalproex may irritate the stomach less than valproic acid.*)
- Weight gain, increased appetite (*this may be more common at higher doses. Try exercising, limiting foods high in calories and eating a healthy and well-balanced diet (see: “Eating Well with Canada’s Food Guide”)*)
- Mild skin rash, itchy skin (*try using a special anti-itch moisturizer (e.g. Aveeno®)*)

### Uncommon side effects (e.g. those that occur in less than 5% of patients)

There are risks involved with taking any medication. Make sure you have had a conversation with your doctor about the potentially serious effects of valproic acid.



### **Contact your doctor IMMEDIATELY if you have any of these side effects:**

- Aggression, hyperactivity, irritability, agitation, nervousness or any other unusual changes in behaviour
- Easy bruising or bleeding from the skin or other areas
- Increased frequency of seizures
- Loss of appetite, abdominal pain, severe nausea or vomiting
- Swelling in the face, ankles, feet or lower legs or severe skin rash
- Thoughts of self-harm, hostility or suicide
- Yellow skin or eyes, itchiness, loss of appetite, weakness, vomiting, dark colored urine, or pain in the upper right part of the abdomen
- In females: acne, abnormal hair growth, irregular menstrual periods, inability to become pregnant (when this is desired), excessive weight gain

## What precautions should my doctor and I be aware of when taking valproic acid?

Many medications can interact with valproic acid, including blood-thinning medications such as acetylsalicylic acid (Aspirin®) and warfarin (Coumadin®); mood stabilizers such as lamotrigine (Lamictal®) and carbamazepine (Tegretol®); anticonvulsants such as phenytoin (Dilantin®); antidepressants such as amitriptyline (Elavil®) and fluoxetine (Prozac®);

some anti-anxiety medications such as clonazepam (Rivotril®); antibiotics such as erythromycin; cimetidine (Tagamet®), and several others. If you are (or begin) taking any other prescription or over-the-counter medications, be sure to check with your doctor or pharmacist to see if they are safe to use. Your doctor may need to change the doses of your medication(s) or monitor you carefully for side effects if you are taking certain other medications.

Tell your doctor or pharmacist if you:

- have any allergies or have experienced a reaction to a medication
- have a history of pancreas, kidney or liver problems
- have a history of polycystic ovarian syndrome (presence of cysts in the ovaries)
- have a history of seizures (epilepsy)
- have a history of blood disorders
- have a history of serious skin reactions
- have a history of urea cycle disorders (a genetic disorder)
- have a history of brain conditions (e.g. unexplained coma, intellectual disability or any brain dysfunction)
- currently or in the past, have had thoughts/attempts of suicide or self-harm
- have hallucinations (seeing or hearing things that are not there)
- use alcohol on a regular basis or have a history of alcohol abuse
- Miss a period, are pregnant, or are trying to become pregnant or are breast-feeding. Tell your doctor right away if you become pregnant while taking valproic acid

### **What special instructions should I follow while using *valproic acid*?**

- Keep all appointments with your doctor and the laboratory. Your doctor may order certain lab tests (valproic acid blood levels, liver function tests, platelet count, complete blood cell counts) to check for side effects and how you are responding to valproic acid.
- Try to keep a healthy and well-balanced diet and exercise regularly. Some individuals who take valproic acid may gain weight due to an increase in appetite.
- Do not allow anyone else to use your medication.

### **What should I do if I forget to take a dose of *valproic acid*?**

If you take valproic acid regularly and you forget to take it, take it as soon as you remember. If it is more than 4 hours after your regularly scheduled dose, skip the missed dose and continue with your regular schedule. Do NOT double your next dose.



### **What storage conditions are needed for *valproic acid*?**

- Keep this medication in the original container, stored at room temperature away from moisture and heat (e.g., not in the bathroom or kitchen).
- Keep this medication out of reach and sight of children.

You may wish to share this information with your family members to help them to understand your treatment options. Since every person's needs are different, it is important that you follow the advice provided to you by your own doctor, nurse and/or pharmacist and speak to them if you have any questions about this medication.

*Developed by the health care professionals of the Child & Adolescent Mental Health Program and reviewed by the staff of the Kelty Mental Health Resource Centre.*