

PART III: CONSUMER INFORMATION

^{Pr}EPIVAL[®] enteric-coated tablets divalproex sodium

This leaflet is PART III of a three-part "Product Monograph" published when EPIVAL[®] was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about EPIVAL[®]. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

EPIVAL[®] has been prescribed to you to either:

- control your epilepsy
- treat symptoms of mania associated with bipolar disorder, such as aggressiveness, agitation, impulsive behaviour or excessively elevated mood.

EPIVAL[®] is not indicated for the treatment of the symptoms of mania in patients under 18 years of age.

Please follow your doctor's recommendations carefully.

What it does:

EPIVAL[®] has anticonvulsant properties. The mechanism of action has not yet been established. It has been suggested that its activity in epilepsy is related to increased brain concentrations of gamma-aminobutyric acid (GABA).

When it should not be used:

EPIVAL[®] should not be taken by:

- patients with liver disease or significant liver dysfunction
- patients who are allergic to the drug
- patients with known urea cycle disorders (a genetic disorder)

What the medicinal ingredient is:

divalproex sodium

What the non-medicinal ingredients are:

EPIVAL[®] 125 mg tablets also contain diacetylated monoglycerides, FD&C Red No. 40, hydroxypropylmethyl cellulose phthalate, povidone, pregelatinized starch (contains corn starch), silicon dioxide, talc, titanium dioxide, and vanillin.

EPIVAL[®] 250 mg tablets also contain diacetylated monoglycerides, FD&C Yellow No. 6, hydroxypropylmethyl cellulose phthalate, povidone, pregelatinized starch (contains corn starch), silicon dioxide, talc, titanium dioxide, and vanillin.

EPIVAL[®] 500 mg tablets also contain diacetylated monoglycerides, D&C Red No. 30, FD&C Blue No. 2, hydroxypropylmethyl cellulose phthalate, povidone, pregelatinized starch (contains corn starch), silicon dioxide, talc, titanium dioxide, and vanillin.

For a full listing of non-medicinal ingredients see PART I of the Product Monograph.

What dosage forms it comes in:

EPIVAL[®] is available as enteric-coated tablets in the following strengths: 125 mg, 250 mg, and 500 mg.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- **Hepatotoxicity:** liver failure resulting in death has occurred in patients receiving EPIVAL[®]. These incidents usually occurred during the first 6 months of treatment with EPIVAL[®]. Patients taking several anticonvulsant drugs, children, those with a history of liver disease, metabolic disorders, severe seizure disorders accompanied by mental retardation, and those with brain disease may be at particular risk. Experience has indicated that children under the age of 2 years are at a considerably increased risk of developing fatal hepatotoxicity, especially those on multiple anticonvulsants.
- **Teratogenicity:** EPIVAL[®] can produce birth defects to an unborn baby. Accordingly, the use of EPIVAL[®] in women of childbearing potential requires that the benefits of its use be weighed against the risk of injury to the fetus.
- **Pancreatitis:** cases of life threatening pancreas disorder have been reported in both children and adults receiving EPIVAL[®]. Some cases have occurred shortly after first use as well as after several years of use. Abdominal pain, nausea, vomiting and/or anorexia can be symptoms of pancreatitis that require immediate medical evaluation.

BEFORE you use EPIVAL[®] talk to your doctor or pharmacist if:

- you have a history of, or suffer from a liver disease, such as jaundice (yellowing of the skin and eyes);
- you ever had an unusual or allergic reaction to EPIVAL[®] (including fever or rash);
- you are allergic to any component of EPIVAL[®] tablets;
- you are pregnant or are planning to become pregnant;
- you are breast-feeding (nursing); EPIVAL[®] passes into breast milk;
- you are taking any other prescription or over the counter medicine-;
- you have kidney disease;
- you have other medical conditions including a history of unexplained coma, mental retardation or any type of brain dysfunction;

- you have a psychiatric disorder or have thoughts of suicide;
- you consume alcohol on a regular basis.

Precautions while taking EPIVAL®:

- Your doctor will monitor your response to EPIVAL® on a regular basis. However, if your seizures get worse, you should tell your doctor immediately.
- Since EPIVAL® may cause poor coordination and/or drowsiness, you should not engage in hazardous activities, such as driving and operating machinery, until you know that you don't become drowsy from the drug.
- You should not stop taking your medication unless directed by your doctor. You should always check that you have an adequate supply of EPIVAL®. You should remember that this medicine was prescribed only for you; it should never be given to anyone else.

The doctor may need to take blood tests to measure the amount of EPIVAL® in your blood when adjusting your medications.

Usual dose:

It is very important to take EPIVAL® exactly as instructed by your doctor.

The recommended starting dose of EPIVAL® will be decided by your doctor based on your weight, your seizures or manic episodes and your concomitant medications. Be sure to tell your doctor all the prescription and over the counter medications that you are currently taking. Your doctor will gradually increase the dosage until your condition is well controlled without experiencing side effects. You should carefully follow the instructions that were given to you and not change your dose without consulting with your doctor.

EPIVAL® may be taken with or without food.

EPIVAL® is not indicated for the treatment of the symptoms of mania in patients under 18 years of age.

Overdose:

If you accidentally take an overdose of EPIVAL®, you should contact your doctor or nearest hospital emergency, or your Regional Poison Control Centre, even though you may not feel sick.

Missed Dose:

Do not abruptly stop taking your medicine because of the risk of increasing your epileptic seizures.

If you miss a dose, you should not try to make up for it by doubling up on your next dose. You should take your next regularly scheduled dose and try not to miss any more doses.

INTERACTIONS WITH THIS MEDICATION

Serious Drug Interactions

- Rare cases of coma have been reported in patients receiving EPIVAL® alone or when taken with phenobarbital.
- Serious skin reactions (such as conditions called Stevens-Johnson syndrome and Toxic Epidermal Necrolysis) have been reported when EPIVAL® and lamotrigine were taken together.

Drugs that may interact with EPIVAL® include:

- anticonvulsants such as carbamazepine, lamotrigine, primidone, topiramate, felbamate, phenytoin, ethosuximide, phenobarbital;
- anticoagulants such as acetylsalicylic acid, warfarin, dicumarol;
- benzodiazepines such as diazepam, lorazepam, clonazepam;
- some medicines used to treat infections such as rifampin;
- some medicines used to treat diabetes such as tolbutamide;
- some HIV-antiviral medication such as zidovudine;
- any of the group of antibiotics in the carbapenem class such as doripenem, ertapenem, imipenem, meropenem;
- some medicines used to treat heartburn and peptic ulcers such as cimetidine;
- medicines used to treat depression such as Selective Serotonin Re-Uptake Inhibitors (SSRIs), Monoamine Oxidase Inhibitors (MAOIs), Tricyclic antidepressants such as amitriptyline, nortriptyline;
- antipsychotics.

PROPER USE OF THIS MEDICATION

Please consult your doctor before taking any other medication, including over-the-counter medicines. Some drugs can produce various side effects when they are used in combination with EPIVAL®.

It is important to keep your appointments for medical checkups.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

You should check with your doctor or pharmacist right away if you notice any bothersome or unusual effects while taking EPIVAL®.

Different side effects have been reported by patients taking EPIVAL®. The most commonly reported adverse reactions are nausea, vomiting and indigestion. You should know that this does not mean that you will experience such effects, because people can react in different ways to the same medicine.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/effect		Talk with your doctor or pharmacist right away		Seek emergency medical attention
		Only if severe	In all cases	
Common	Nausea	✓		
	Vomiting	✓		
	Indigestion	✓		
	Sedation	✓		
	Headache	✓		
	Diarrhea	✓		
Uncommon	Brain dysfunction with high blood ammonia levels (increased lethargy/drowsiness, vomiting, ataxia [abnormal gait, abnormal walking], episodes of extreme irritability [†] , combative/bizarre behaviour ^{††} and refusal to eat meat or high protein products ^{††})		✓	
	Decreased number of platelets in the blood (may result in easy bruising and bleeding from the skin or other areas)		✓	
	Liver disorder (not feeling well, develop weakness, lethargy, facial swelling, loss of appetite, yellowing of the skin or eyes, dark urine, and vomiting)		✓	
	Pancreas disorder (abdominal pain, nausea, vomiting, and/or loss of appetite)		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/effect		Talk with your doctor or pharmacist right away		Seek emergency medical attention
		Only if severe	In all cases	
	Thoughts of suicide or hurting yourself		✓	

[†] In young children
^{††} In older children or adults

This is not a complete list of side effects. For any unexpected effects while taking EPIVAL[®], contact your doctor or pharmacist.

HOW TO STORE IT

EPIVAL[®] tablets should be stored between 15 and 25°C. Tablets should be protected from light.

EPIVAL[®] should be kept out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report on line at:**
<http://www.healthcanada.gc.ca/medeffect>
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
 - **Fax toll-free to 1-866-678-6789**
 - **Mail to: Canada Vigilance Program
 Health Canada
 Postal Locator 0701C
 Ottawa, ON K1A 0K9**

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect[™] Canada Web site at <http://www.healthcanada.gc.ca/medeffect>

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full Product Monograph, prepared for health professionals can be found at

<http://www.abbott.ca>

or by contacting the sponsor, Abbott Laboratories, Limited,
Saint-Laurent, Qc H4S 1Z1 at:
1-800-699-9948

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