PART III: CONSUMER INFORMATION

PrDEPAKENE®
valproic acid oral solution

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

ABOUT THIS MEDICATION

What the medication is used for:

- DEPAKENE® has been prescribed to you to control your epilepsy. Please follow your doctor's recommendations carefully.

What it does:

DEPAKENE® 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:

DEPAKENE® should not be taken by:

- patients with liver disease or significant liver dysfunction
- patients with mitochondrial diseases (e.g., Alpers or Alpers-Huttenlocher disease)
- patients who are allergic to valproic acid or any of the other ingredients in DEPAKENE®
- patients with known urea cycle disorders (a genetic disorder)
- patients with porphyria (a genetic disorder)

What the medicinal ingredient is:

valproic acid

What the non-medicinal ingredients are:

DEPAKENE® 250 mg/5 mL oral solution contains the following non-medicinal ingredients: artificial cherry flavor, dye red FD&C No. 40, glycerin, methylparaben*, propylparaben*, purified water, sorbitol, sucrose, vanillin, and hydrochloric acid and sodium hydroxide for pH adjustment.

* methylparaben and propylparaben may cause allergic reactions (possibly delayed).

What dosage forms it comes in:

DEPAKENE® is available as an oral solution containing 250 mg of valproic acid for every 5 mL.

DEPAKENE® is also available as a capsule containing 250 mg of valproic acid.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- **Hepatotoxicity:** liver failure resulting in death has occurred in patients receiving DEPAKENE®. These incidents usually occurred during the first 6 months of treatment with DEPAKENE®. 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.
- **Birth Defects:** DEPAKENE® can cause birth defects and problems with early development of the child if it is taken during pregnancy. DEPAKENE® should not be used in female children, in female adolescents, in women of childbearing potential and pregnant women unless other treatments do not work or are not tolerated. If you are a female of childbearing age you should use an effective method of birth control while you are taking DEPAKENE®. Tell your doctor right away if you become pregnant or think you might be pregnant.
- **Pancreatitis:** cases of life threatening pancreas disorder have been reported in both children and adults receiving DEPAKENE®. 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 DEPAKENE® 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);
- have ever had an unusual or allergic reaction to DEPAKENE® (including fever or rash);
- are a female child or female adolescent, a woman of childbearing potential, or pregnant;
- are breast-feeding (nursing); DEPAKENE® passes into breast milk. You must discuss with your doctor whether you should breastfeed or take DEPAKENE®. You cannot do both;
- are male and thinking about fathering a child. DEPAKENE® can make you less fertile;
- are taking any other prescription or over the counter medicine;
- have kidney disease;
- have other medical conditions including a history of unexplained coma, intellectual disability or any type of brain dysfunction;
- have a psychiatric disorder or have thoughts of suicide;
- consume alcohol on a regular basis.

Precautions while taking DEPAKENE®:

- Your doctor will monitor your response to DEPAKENE® on a regular basis. However, if your seizures get worse, you should tell your doctor immediately.
- Since DEPAKENE® 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 DEPAKENE®. You should remember that this medicine was prescribed only for you; it should never be given to anyone else.
- As with other drugs used to treat epilepsy, some patients may experience an increase in the number of seizures and the severity (including status epilepticus), or the onset of new types of seizures with DEPAKENE® instead of an improvement. If your start having more seizures, new types of seizures or your seizures get worse contact your doctor immediately.

Female Children, Female Adolescents and Women of Childbearing Potential

- All female children, female adolescents and women of childbearing age who are being treated with DEPAKENE® should talk to their healthcare providers about using other possible treatments instead of DEPAKENE®. If you are a female capable of becoming pregnant you should only take DEPAKENE® if nothing else works for you. If the decision is made to use DEPAKENE®, you must use an effective method of birth control (contraception). You should talk to your doctor about the best kind of birth control to use while you are taking DEPAKENE®.
- No longer getting your period, fluid filled sacs (cysts) on the ovaries and increased testosterone levels have been reported in women taking DEPAKENE®.
- Before prescribing this medicine to you, your doctor will have explained what might happen to your baby if you become pregnant while taking DEPAKENE®. If you decide later you want to have a child you should not stop taking your medicine until you have discussed this with your doctor and agreed on a plan for switching to another medication if this is possible.
- Ask your doctor about taking folic acid when trying to get pregnant. Folic acid can lower the general risk of birth defects in the spine (spina bifida) and early miscarriage that exists with all pregnancies. However, it is unlikely that folic acid will reduce the risk of birth defects associated with DEPAKENE® use.

Pregnant Women

- DEPAKENE® carries a risk if taken during pregnancy. The higher the dose, the higher the risks, though all doses carry a risk.
- If you take DEPAKENE ® during pregnancy, your child has a serious risk of birth defects and problems with development which can be seriously debilitating such as lower IQ and problems with brain development. Birth defects which have been reported include spina bifida (where the bones of the spine are not properly developed); problems with the development of the bones of the face and skull; and problems with the development of the heart, kidney, urinary tract and sexual organs, arms and legs. These can begin early in the pregnancy, even before you know that you are pregnant.
- It is estimated that up to 30-40% of preschool children whose mothers took DEPAKENE® during pregnancy may have problems with early childhood development. This means these children can be slow to walk and talk, have lower intelligence (lower IQ scores) than other children, and have difficulty with language and memory.
- Children born to mothers who took DEPAKENE® during pregnancy are also more likely to have Autism spectrum disorders and more likely to develop symptoms of Attention Deficit Hyperactivity Disorder (ADHD).
- There may be other medications to treat your condition that have a lower chance of birth defects.
- If you are planning to become pregnant, or if you become pregnant while taking DEPAKENE®, you should promptly inform your doctor. Do not suddenly stop taking the drug. Appropriate treatment options will need to be discussed with your physician to ensure the benefits outweigh the risks.
- Pregnancy Registry: If you become pregnant while taking DEPAKENE ®, talk to your doctor about registering with the North American Antiepileptic Drug Pregnancy Registry. You can enroll in this registry by calling 1-888-233-2334. The purpose of this registry is to collect information about the safety of antiepileptic medicines during pregnancy. Information on the registry can also be found at the following website: http://www.aedpregnancyregistry.org/.

INTERACTIONS WITH THIS MEDICATION

Serious Drug Interactions

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

Drugs that may interact with DEPAKENE® include:

- anticonvulsants such as carbamazepine, lamotrigine, primidone, topiramate, felbamate, phenytoin, ethosuximide, phenobarbital, olanzapine, rufinamide;
- 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, ritonavir, lopinavir, lamivudine;
- 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;
- acetazolamide a medicine used to treat glaucoma and epilepsy;
- cholestyramine, a medicine used to lower cholesterol;
- propofol, a drug used to relax you before and after surgery;
- nimodipine;
- antipsychotics;
- estrogen-containing products (including contraceptives that contain estrogen).

PROPER USE OF THIS MEDICATION

DEPAKENE® treatment must only be started and supervised by a doctor specialised in the treatment of epilepsy. 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 DEPAKENE®.

It is important to keep your appointments for medical checkups.

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

Do not stop taking DEPAKENE® suddenly as this can cause a serious increase in the number of seizures and their severity, including status epilepticus.

Usual dose:

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

The recommended starting dose of DEPAKENE® will be decided by your doctor based on your weight, your seizures 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.

DEPAKENE® may be taken with or without food.

Overdose:

If you think you have taken too much DEPAKENE®, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

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.

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 DEPAKENE®.

The most commonly reported adverse reactions include nausea, vomiting, indigestion sleepiness, headache, diarrhea, weakness, tremor and dizziness. Changes in hair are also reported, such as hair loss or in increase in hair on face, chest and back. If any of these affect you severely, contact your doctor or pharmacist.

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	**Hallucinations:** seeing or hearing something that is not there	√		
	Urinary incontinence		√	
Uncommon	**Brain dysfunction from high ammonia levels in the blood:** tiredness, vomiting, abnormal walking, extreme irritability†, combative/bizarre behaviour††, 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		√	

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	
	Liver disorder: weakness, tiredness, abdominal pain, diarrhea, facial swelling, loss of appetite, yellowing of the skin or eyes, dark urine, nausea, and vomiting		√	
	Pancreas disorder: abdominal pain, nausea, vomiting, and/or loss of appetite		√	
	Thoughts of suicide or hurting yourself: symptoms of depression or unusual changes in mood or behaviour		√	
Rare	**Muscle disorder:** unexplained muscle pain or tenderness, with a fever or "tea-coloured" urine, or reduced urination		√	

† In young children
†† In older children or adults

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

HOW TO STORE IT

Store DEPAKENE® oral solution between 15 and 30ºC.

DEPAKENE® 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:** 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 0701E
    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

The most recent version of this document plus the full Product Monograph, prepared for health professionals can be found at:

www.mylan.ca
or by contacting the sponsor, BGP Pharma ULC, Etobicoke, Ontario, M8Z 2S6 at:
1-844-596-9526

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