PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrDEPAKENE®

valproic acid oral solution

Read this carefully before you start taking **DEPAKENE®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **DEPAKENE®**.

Serious Warnings and Precautions

- **Birth Defects and development disorders:**
  - DEPAKENE® can cause birth defects in your child if you take it during pregnancy, including when valproate is used in combination with other medicines to treat epilepsy. These birth defects can seriously affect your child and result in disabilities which can be severe. The most frequently reported birth defects include:
    - *spina-bifida* (a condition where the bones of the spine are not properly developed);
    - problems with the development of the bones of the face and skull;
    - heart, kidney, urinary and sexual organ malformations; limb defects;
    - multiple associated malformations affecting several organs and parts of the body (including eye malformations. These eye malformations may affect vision);
    - hearing problems or deafness;
  - If you take DEPAKENE® during pregnancy, alone or together with other epilepsy medicines, it can affect the physical and mental development of the child as it grows after birth, including the following:
    - problems with early childhood development such as slow to walk and talk, lower IQ or problems with brain development;
    - autism or autism spectrum disorders;
    - Attention Deficit Hyperactivity Disorder (ADHD)

  These can begin early in the pregnancy, even before you know that you are pregnant. DEPAKENE® should not be used in female children, in women of childbearing potential or in pregnant women unless your doctor decides that you should. If you are taking DEPAKENE® and are of childbearing potential, you should use an effective method of birth control. If you become pregnant, or think you may be pregnant while taking DEPAKENE®, tell your doctor **right away**.
- **Liver Failure:** cases of fatal liver failure have occurred in patients receiving DEPAKENE®. If liver failure occurs, it usually happens during the first 6 months of treatment. You are more at risk for liver failure if you:
  - take other drugs used to treat seizures

- are a child (especially a child under 2 years of age taking multiple drugs to treat seizures)
- have a history of liver disease
- were born with a metabolic disorder (including mitochondrial disorders)
- have seizures with an intellectual disability
- have brain disease

- **Mitochondrial Disorders:** if you or your child have a mitochondrial disorder such as Alpers Huttenlocher Syndrome, do not take DEPAKENE®. If your child is under 2 years of age and you think they may have a mitochondrial disorder, they should not be given DEPAKENE® unless all other medications have failed.
- **Pancreatitis** (inflammation of the pancreas): cases of life-threatening pancreatitis have occurred in both children and adults taking DEPAKENE®. Some instances happen shortly after the first use of DEPAKENE®, while others after several years of use. Talk to your healthcare professional right away if you start to have any symptoms of pancreatitis.

  (See the **Serious side effects and what to do about them** table below for symptoms of liver failure and pancreatitis).

What is DEPAKENE® used for?

- DEPAKENE® is used in adults and children to control epilepsy (a disorder of the brain that causes seizures. Please follow your doctor's instructions carefully.

How does DEPAKENE® work?

DEPAKENE® is thought to work by increasing the amount of an amino acid in the brain called "gamma-aminobutyric acid" (GABA). By changing the amount of GABA in the brain, DEPAKENE® is able to help control epilepsy.

What are the ingredients in DEPAKENE®?

Medicinal ingredients: valproic acid

Non-medicinal ingredients: artificial cherry flavor, FD&C Red No. 40, glycerin, methylparaben*, propylparaben*, purified water, sorbitol, sucrose, vanillin, and hydrochloric acid and sodium hydroxide for pH adjustment.

* methylparaben and propylparaben may cause an immediate or delayed allergic reaction.

DEPAKENE® comes in the following dosage forms:

Oral solution; 250 mg of valproic acid for every 5 mL.

Do not use DEPAKENE® if:

- you are allergic to valproic acid or to any other ingredient in DEPAKENE®
- you are pregnant, think you are pregnant or are planning to become pregnant, unless you and your doctor have decided you should

- you are a girl or woman of childbearing potential, unless you meet all conditions of the **Pregnancy Prevention Program**, your doctor will talk to you about this
- you have liver disease or severe liver problems
- you have a mitochondrial disorder, such as Alpers-Huttenlocher Syndrome. Children under 2 years of age who may have a mitochondrial disorder should not take DEPAKENE®
- you have or have a family history of a urea cycle disorder (a condition that affects how your body removes waste)
- you have an inborn deficiency in carnitine that is untreated
- you have porphyria (a condition that affects the nervous system and skin)
- you or any of your close relatives have a history of severe hepatitis, especially when caused by medicines

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take DEPAKENE®. Talk about any health conditions or problems you may have, including if you:

- have or have a history of liver disease or liver problems;
- are breastfeeding or planning to breastfeed. You must discuss with your doctor whether to breastfeed or take DEPAKENE®, you cannot do both. Do not breastfeed for one month after stopping DEPAKENE®;
- have kidney disease or kidney problems;
- have diabetes;
- have any of the following rare conditions, DEPAKENE® contains sucrose:
  - fructose intolerance
  - glucose-galactose malabsorption
  - sucrose-isomaltase insufficiency
- have Human Immunodeficiency Virus (HIV) or Cytomegalovirus (CMV);
- have a history of muscular disorders (including carnitine palmitoyltransferase type II deficiency);
- are on a diet with low carnitine (found in meat and dairy products), especially in children;
- have an inborn deficiency in carnitine and are taking carnitine supplement for this condition;
- have other medical conditions including a history of unexplained coma, intellectual disability or any type of brain dysfunction;
- drink alcohol on a regular basis;
- are elderly (65 years of age or older).

Other warnings you should know about:

Pregnancy: DEPAKENE® may harm your unborn baby. Your doctor may require you to do a pregnancy test before you start treatment with DEPAKENE® to make sure that you are not pregnant. **You must use effective methods of birth control.** It is recommended that you use a form of birth control that does not depend on you to remember to use or take it, such as an intrauterine device (IUD) or 2 forms of birth control, such as the pill and a condom. You should use birth control:

- for at least one month before starting DEPAKENE®;
- while you are taking DEPAKENE®;
- for at least one month after stopping DEPAKENE®.

Talk to your doctor about the best form of birth control for you. Some hormonal birth controls that contain estrogen may affect how well DEPAKENE® works.

Before prescribing DEPAKENE®, your doctor should have explained to you what might happen to your baby if you become pregnant while taking DEPAKENE® (see the **Serious warnings and precautions** box above). If you are a parent or caring for a female child taking DEPAKENE®, tell the doctor as soon as your child has her first period. If you have any questions about what may happen if you become pregnant, talk to a healthcare professional. If you become pregnant, or think you are pregnant while taking DEPAKENE®, tell your doctor **right away**.

When you are prescribed DEPAKENE®:

- your doctor will give you a patient guide;
- you should receive a patient card every time you get DEPAKENE® from the pharmacy.

Make sure you understand these documents.

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/.

Pregnancy Prevention Program: Information on the Pregnancy Prevention Program including educational resources, as well as to report suspected embryo-fetal exposure to valproate, can be found at the following website: www.depakene.ca.

Fertility:

Use in Women: If you are female and taking DEPAKENE® you may no longer get your period. You may also develop cysts (fluid filled sacs) on the ovaries and your testosterone levels may increase.

Use in Men: DEPAKENE® may affect male fertility during treatment. DEPAKENE® can make you less fertile or infertile. This **may or may not** be reversible if your dose is decreased or if you stop taking DEPAKENE®.

If you have interest in starting a family, talk to your doctor. Do not stop taking DEPAKENE® unless your doctor has told you to do so.

Monitoring and Blood Tests: Your doctor should do blood tests before starting treatment with DEPAKENE® and while you are taking it. These tests may monitor:

- platelet (a type of blood cell) count and your blood's ability to clot
- liver function
- the amount of valproate (the active ingredient in DEPAKENE®) in the body
- the amount of any other medications you are taking in your body
- sugar (glucose) levels in your blood
- ammonia levels in your blood

Your doctor will monitor your response to DEPAKENE® on a regular basis. If you start to have more seizures or your seizures get worse, tell your doctor immediately.

Suicidal Thoughts and Behaviour Changes: If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital right away. DEPAKENE® may also cause behavioural changes in you or your child such as aggression, agitation, change in attention span and learning disorders.

Driving and Using Machines: DEPAKENE® may cause you to become drowsy or light-headed. Avoid driving, using machinery, or doing dangerous activities until you know how DEPAKENE® affects you.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with DEPAKENE®:

- **phenobarbital and lamotrigine, which are anticonvulsants (drugs used to treat seizures). These might cause serious life-threatening effects when mixed with DEPAKENE®;**
- other anticonvulsants such as carbamazepine, primidone, topiramate, felbamate, phenytoin, ethosuximide, rufinamide;
- anticoagulants (drugs used to thin blood) such as warfarin, dicumarol;
- acetylsalicylic acid (aspirin); especially if your child is under 3 years of age, DEPAKENE® should not be administered together with acetylsalicylic acid;
- 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 medicines such as zidovudine, ritonavir, lopinavir, lamivudine;
- 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 drug used to treat glaucoma and epilepsy;
- cholestyramine, a drug used to lower cholesterol;
- propofol, a drug used to relax you before and after surgery;
- nimodipine, a drug used to prevent brain damage;
- metamizole (used to treat pain and fever; not approved in Canada for human use);
- methotrexate (used to treat cancer and inflammatory diseases);
- some medicines that contain pivalate (e.g. adefovir dipivoxil);
- antipsychotics (drugs used to manage psychosis) such as olanzapine, chlorpromazine, quetiapine;
- estrogen-containing products (including contraceptives that contain estrogen);
- alcohol
- cannabidiol (CBD).

How to take DEPAKENE®:

- DEPAKENE® treatment must only be started and supervised by a doctor specialised in the treatment of epilepsy.
- It is important to keep your appointments for medical checkups.

- Take DEPAKENE® exactly as your doctor prescribes, do not change your dose unless your doctor tells you to.
- Do not stop taking DEPAKENE® suddenly as this can increase the number of seizures you have and their severity, including status epilepticus.
- DEPAKENE® can be taken with or without food.

Usual dose:

Your doctor will decide the dose of DEPAKENE® for you. The dose is based on your weight, your seizures and the other medicines you or your child take. Your doctor will slowly increase the dosage until your or your child's condition is well controlled, without side effects.

Overdose:

If you think you, or a person you are caring for, have taken too much DEPAKENE®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you or your child misses a dose, do not try to make up for it by doubling the next dose. Take or give the next regularly scheduled dose and try not to miss any more doses.

What are possible side effects from using DEPAKENE®?

These are not all the possible side effects you or your child may have when taking DEPAKENE®. If you or your child experience any side effects not listed here, tell your healthcare professional.

- headache
- nausea or vomiting
- indigestion
- diarrhea
- tremors (involuntary shaking)
- feeling tired
- feeling weak or dizzy
- hair loss or hair growth on the face, chest or back
- increased appetite that may lead to weight gain

Additional side effects in children:

Compared to adults, some side effects of **DEPAKENE®** occur more frequently and/or are more severe in children. These include liver damage, inflammation of the pancreas (pancreatitis), aggression, agitation, disturbance in attention, abnormal behavior, hyperactivity and learning disorder.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Get immediate medical help**
	Only if severe	**In all cases**	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
COMMON			
Allergic reaction: difficulty swallowing or breathing, wheezing; drop in blood pressure; feeling sick to your stomach and throwing up; hives or rash; swelling of the face, lips, tongue or throat.			X
Hallucinations (seeing or hearing things that are not there)	X		
Urinary incontinence (involuntary loss of urine)		X	
UNCOMMON			
Aggravated convulsions (an increase in the number of seizures you have or having new types of seizures)			X
Depression (sad mood that won't go away): difficulty sleeping or sleeping too much, changes in appetite or weight, feelings of worthlessness, guilt, regret, helplessness or hopelessness, withdrawal from social situations, family, gatherings and activities with friends, reduced libido (sex drive) and thoughts of death. If you have a history of depression, your depression may become worse		X	
Hyperammonemia (high ammonia levels in the blood): tiredness, vomiting, abnormal walking, extreme irritability, combative/bizarre behaviour, not wanting to eat meat or high protein products			X
Hypothermia (low body temperature): shivering, slurred speech or mumbling, slow, shallow breathing, weak pulse, very low energy, confusion or memory loss		X	
Kidney problems: nausea,		X	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
vomiting, fever, swelling of extremities, fatigue, thirst, dry skin, irritability, dark urine, increased or decreased urine output, blood in the urine, rash, weight gain (from retaining fluid), loss of appetite, abnormal blood test results, mental status changes (drowsiness, confusion, coma)			
Liver injury: yellowing of the skin or eyes, itchy skin, dark urine and pale stools, abdominal pain, nausea, vomiting, loss of appetite			X
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid heart beat, nausea, vomiting, tenderness when touching the abdomen			X
Serious skin reactions when taken with lamotrigine: fever, severe rash, swollen lymph glands, flu-like feeling, blisters and peeling skin that may start in and around the mouth, nose, eyes and genitals and spread to other areas of the body, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine			X
Thoughts of suicide or hurting yourself			X
Thrombocytopenia (low blood platelets): bruising or bleeding for longer than usual if you hurt yourself, fatigue and weakness		X	
RARE			
Brain atrophy (loss of brain cells): memory loss, seizures, loss of motor skills, difficulty speaking, reading or understanding.		X	
Coagulation abnormalities (problems with how your blood		X	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
clots): abnormal bleeding, bruising easily, won't stop bleeding when you are injured, sudden nosebleeds, fatigue, headache			
Fanconi syndrome (kidney does not function properly leading to certain essential substances to exit through urine): passing a lot of urine, feeling thirsty, bone pain, weakness			X
Rhabdomyolysis (breakdown of damaged muscle): muscle tenderness, weakness, red-brown (tea-coloured) urine			X
UNKNOWN FREQUENCY			
Hypocarnitinemia (low carnitine levels in the blood and/or tissues): fatigue, muscle weakness and pain	X		

If you or your child have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store DEPAKENE® oral solution between 15 and 30°C.

Keep out of reach and sight of children.

If you want more information about DEPAKENE®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.mylan.ca, or by calling 1-844-596-9526.

This leaflet was prepared by BGP Pharma ULC.

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