

PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

**Depalept syrup 200 mg/5 ml
Depalept 200 mg enteric-coated tablets
Depalept 500 mg enteric-coated tablets**

Depalept syrup
Sodium Valproate 200 mg/5 ml
Depalept 200 mg
Enteric-coated tablets, each tablet contains: Sodium Valproate 200 mg
Depalept 500 mg
Enteric-coated tablets, each tablet contains: Sodium Valproate 500 mg

Inactive ingredients and allergens in the preparation – see section 6 and section 2 "Important information about some of the ingredients of the medicine".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any other questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

The medicine is not intended for children weighing less than 17 kg.

Warning

Depalept may severely harm the fetus when taken during pregnancy

Neonates born to mothers who have taken valproate during pregnancy are at an increased risk of serious developmental disorders (mental and physical) and behavioral disorders (approximately 30-40% of cases) and/or congenital malformations (approximately 11% of cases).

If you are a woman of childbearing age or if you are pregnant, the doctor will prescribe valproate for you only if other treatments are unsuitable.

Women of childbearing age should use effective contraception while taking this medicine. If despite using contraception you become pregnant unintentionally, contact your doctor immediately in order to discuss the options for alternative therapy, if possible. Do not stop using the medicine without consulting the treating doctor, because your condition may worsen.

In addition to the leaflet, the Depalept preparation has a patient safety information card. This card contains important safety information that you must know before starting treatment with Depalept and during the treatment, and act accordingly. Please review the patient information card and the patient leaflet before starting to use the preparation. You should keep the card for further review, if necessary.

1. What is the medicine intended for?

This medicine is an anticonvulsant, and it is administered for treatment of certain types of epilepsy.

Therapeutic class: The active ingredient belongs to the group of anticonvulsants.

2. Before using the medicine:

Do not use this medicine if you:

- Are sensitive (allergic) to the active ingredient or to any component of the medicine (see section 6 – Additional information).
- Are sensitive to another medicine of the valproate family (valproate semisodium, valpromide).
- Have a liver disease (acute or chronic hepatitis).
- Or someone in your family have had or currently has a serious liver disease, especially if it was caused by the use of medications.
- Have hepatic porphyria (a hereditary liver disease).
- Have a genetic problem causing a mitochondrial disorder, e.g. Alpers-Huttenlocher syndrome.
- Have a metabolic disorder, such as urea cycle disorder.
- Are currently taking any of the following medicines:
 - St. John's Wort (for treatment of depression).

Special warnings regarding the use of the medicine

- Do not give this medicine to girls, adolescent girls, women of childbearing age and pregnant women, unless alternative treatments have been found to be unsuitable.
- Women of childbearing age who are treated with this medicine should use effective contraception. If a woman taking this medicine plans to become pregnant, she should consult her doctor regarding the possibility of receiving an alternative treatment.

This medicine may, in very rare cases, cause damage to the liver (hepatitis) or pancreas (pancreatitis), which may be severe and life-threatening.

Your doctor will refer you to perform blood tests for evaluation of liver function, especially during the first 6 months of treatment.

You should consult a doctor immediately if the following effects appear:

- Sudden tiredness, loss of appetite, fatigue, drowsiness, swelling in the legs, general weakness.
- Repeated vomiting, nausea, abdominal pain, yellowing of the skin or the whites of the eyes (jaundice).
- Recurrence of epileptic seizures, even though you are taking the medicine correctly.

Before treatment with Depalept, inform your doctor if:

- You suffer from a kidney disease (renal insufficiency), systemic lupus erythematosus or hereditary enzyme deficiency, especially enzyme deficiency in the urea cycle which may cause elevation of ammonium blood levels, or a genetic problem that causes a mitochondrial disorder (including members of your family).
- Before undergoing any type of surgery, inform the medical staff that you are taking Depalept.
- Before starting treatment, the doctor will check that you are not pregnant and that you are using contraception.
- As with other antiepileptic medicines, taking this medicine may worsen the seizures or increase their frequency. You may even experience a different kind of seizures. If these effects occur, consult a doctor immediately.
- This medicine may cause weight gain. Consult your doctor regarding methods for maintaining normal body weight.
- Taking anticonvulsants may increase the risk for suicidal actions or thoughts. You and your family members must pay attention to changes in mood, behavior patterns and actions. Watch for signs indicating risk of suicide, such as: talking or thinking about wanting to hurt yourself, introversion and withdrawal from family and friends, depression or worsening of existing depression, preoccupation with the subject of death, abandoning or giving away prized possessions. If thoughts of this kind occur, refer to the doctor immediately.
- If you suffer from carnitine palmitoyltransferase (CPT) type II enzyme deficiency (hereditary muscular disease), there is an increased risk of muscle breakdown when taking Depalept.

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- If you suffer from carnitine palmitoyltransferase (CPT) type II enzyme deficiency (hereditary muscular disease), there is an increased risk of muscle breakdown when taking Depalept.

- Medicines containing lithium (for mood stabilization).
- Medicines containing metamazole/dipyron (for treatment of fever and pain).
- Salicylates (including aspirin).
- Cannabidiol (for treatment of epilepsy and other diseases).

Especially in children under the age of 3, avoid the use of medicines containing salicylates (including aspirin) during the treatment with the medicine.

Use of the medicine and food

It is best to take the medicine during meals.

Use of the medicine and alcohol consumption

Drinking alcoholic beverages is not recommended during treatment with this medicine.

Drug interactions

Certain medicines affect the activity of valproate, and vice versa.

Do not take Depalept if you are taking the following medicines:

- St. John's Wort – an herbal remedy for the treatment of depression.
- **Unless the doctor has instructed you otherwise, do not take Depalept if you are taking, have recently taken or may take the following medicines:**
- Lamotrigine (another medicine for the treatment of epilepsy).
- Medicines of the penem group (carbapenems) (a group of antibiotics for treatment of bacterial infections).

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist. Especially if you are taking:

- Medicines containing acetazolamide (for lowering intraocular pressure or carbon dioxide levels in the blood).
- Antibiotics (medicines containing aztreonam or rifampicin).
- Other medicines for the treatment of epilepsy (medicines containing carbamazepine, felbamate, phenytoin, fosphenytoin, primidone, phenobarbital, rufinamide, topiramate or zonisamide).
- Nimodipine - used for prevention of complications that may occur following cerebral bleeding. Depalept may increase the effect of nimodipine.
- Medicines containing estrogen (including certain types of birth control pills).
- Propofol (anesthetic medicine).
- Medicines containing zidovudine (for the treatment of HIV).

Risks of valproate when taken during pregnancy.

- Valproate may harm the fetus when taken during pregnancy. The risk increases with the dosage, **but it exists with all dosages**, even when valproate is taken in combination with other antiepileptic medicines.
- Children exposed to valproate in utero are at high risk for severe congenital malformations and developmental disorders.
- The most common congenital malformations reported include *spina bifida* (a developmental malformation in which the spine does not develop properly), facial, upper lip, palate and skull malformations; malformations of the heart, kidneys, urinary tract and genitals; limb deformities and involvement of multiple other malformations, which affect various organs and

body parts. Congenital malformations may lead to disabilities which may be severe.

- Hearing disorders and hearing impairment have been reported in children exposed to valproate in utero.
- Eye deformities which can affect vision have been reported in children exposed to valproate in utero.

Taking valproate during pregnancy increases the risk of giving birth to a child with congenital malformations that will require medical treatment. It has been found that in women taking valproate, around **11 babies out of 100 are born with congenital malformations, compared with 2-3 babies out of 100 in the general population.**

Approximately 30-40% of pre-school children whose mothers have taken valproate during pregnancy may have problems with early childhood development, such as: delay in starting to walk and talk, lower intellectual ability, language and memory difficulties.

Autistic spectrum disorders are more often diagnosed in children exposed to valproate in utero.

There is some evidence that children exposed to valproate in utero are at an increased risk of developing symptoms of attention deficit hyperactivity disorders (ADHD).

Before giving you the medicine, the doctor will explain to you the possible risks to your baby in the case of exposure to valproate during pregnancy. If you later decide that you wish to become pregnant, do not stop taking the medicine or your contraception before consulting with the doctor and considering the option of changing your treatment, if possible.

Starting treatment with Depalept

If this is the first time Depalept has been prescribed for you, the doctor will explain to you the possible risks for your baby in the case of exposure to valproate during pregnancy. **If you are a woman of childbearing age, you should use effective contraception while using the medicine.** Consult a gynecologist about effective contraception.

Important issues:

- Before starting the treatment, the doctor will make sure that there are no other alternative treatments suitable for you.
- Pregnancy should be ruled out before starting the treatment.
- Make sure that you are using effective contraception.
- A routine follow-up (at least annually) should be carried out by a doctor. The doctor will make sure

that you are aware of and understand the risks and recommendations related to taking valproate during pregnancy.

- If you are planning to become pregnant, inform the doctor before you stop taking your contraception.
- Consult the doctor immediately if you are pregnant or think you might be pregnant.

Continuing Depalept treatment when you are not planning a pregnancy

Make sure you are using effective contraception throughout the treatment period. Consult a gynecologist about effective contraception.

Important issues:

- The treating doctor should routinely (at least annually) evaluate if there are more suitable treatment alternatives for you.
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- Consult the doctor immediately if you are pregnant or think you might be pregnant.

Treatment with Depalept if you are planning a pregnancy

Children exposed to valproate in utero are at high risk for severe congenital malformations and developmental disorders.

To the extent possible, consult your treating doctor before becoming pregnant.

Do not stop using the medicine or your contraception before consulting with your doctor. Your doctor will make every effort to find alternative treatments so that the pregnancy will be as normal as possible, while reducing the risks to you and to the fetus as much as possible.

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