PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

PHEBURANE

GRANULES

The active ingredient and its quantity per dosage unit

Sodium phenylbutyrate 483 mg/g granules

The medicine contains 124 mg of sodium and 768 mg of sucrose for each 1 g of sodium phenylbutyrate.

Inactive and allergenic ingredients in the preparation: see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Further information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or 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.

1. WHAT IS THE MEDICINE INTENDED FOR?

To treat patients with urea cycle disorders. Pheburane is indicated as adjunctive therapy in the chronic management of urea cycle disorders involving deficiencies of carbamylphosphate synthetase, ornithine transcarbamylase or argininosuccinate synthetase enzymes.

The medicine is intended for all newborn patients (with complete enzyme deficiency, presenting within the first 28 days of life). In addition, the medicine is intended for patients with late-onset disease (with partial enzyme deficiency, presenting after the first month of life), who have a history of hyperammonemic encephalopathy.

Therapeutic group: Preparations that affect metabolism.

What is a urea cycle disorder

Urea cycle disorders are due to a deficiency of certain liver enzymes which are necessary to eliminate waste nitrogen in the form of ammonia. Nitrogen is one of the building blocks of proteins, which are an essential part of the food we eat. The body breaks down proteins we eat, but in patients, waste nitrogen in the form of ammonia accumulates because the body cannot eliminate it. Ammonia is toxic to the brain and leads, in severe cases, to a reduced level of consciousness and to coma.

How does Pheburane work

Pheburane helps the body to eliminate waste nitrogen from the body, reducing the amount of ammonia in the body. However, the treatment must be used along with a reduced protein diet, designed especially for you by the doctor and the dietician. You must follow these diet instructions.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient sodium phenylbutyrate or to any of the additional ingredients contained in the medicine (listed in section 6).
- You are pregnant.
- You are breastfeeding.

Special warnings regarding use of the medicine

Before using Pheburane, tell the doctor if:

- You suffer from congestive heart failure (a type of heart disease where the heart cannot pump enough blood around the body) or a decrease in the kidney function.
- You suffer from decreased kidney or liver function, since Pheburane is eliminated from the body through the kidney and liver.

Pheburane will not prevent the occurrence of an acute excess of ammonia in the blood, a condition which generally constitutes a medical emergency situation. If this happens, you will develop symptoms such as nausea, vomiting, confusion and will need to get urgent medical help.

Tests and follow-up

If you need to perform laboratory tests, it is important to remind your doctor that you are taking Pheburane, since the active ingredient sodium phenylbutyrate may interfere with several laboratory test results (such as: blood electrolytes or proteins, or liver function tests).

Drug interactions

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

Especially if you are taking:

- Valproate (a medicine to treat epilepsy).
- Haloperidol (used for certain psychotic conditions).
- Corticosteroids (medicines that are used to relieve inflammation of different body areas).
- Probenecid (intended for treatment of excess uric acid in the blood, associated with gout disease).

These medicines may change the effect of Pheburane and you will need to undergo more frequent blood tests.

If you are uncertain if your medicines contain these substances, check with the doctor or pharmacist.

Pregnancy and breastfeeding

Do not use Pheburane if you are pregnant, since this medicine can harm your unborn baby.

If you are a woman who could get pregnant, **you must use reliable contraception during treatment with Pheburane.** Talk with your doctor for details.

Do not use Pheburane if you are breastfeeding, since this medicine can pass into the milk and may harm your baby.

Driving and operating machinery

Pheburane is not expected to affect your ability to drive and operate machinery.

Important information about some of the ingredients of the medicine

Pheburane contains sodium and sucrose

This medicine contains 124 mg (5.4 mmol) sodium per 1 g of the active ingredient sodium phenylbutyrate. Refer to a doctor if you need 3 g or more per day for a prolonged period, especially if you are on a salt (sodium)-controlled diet.

This medicine contains 768 mg sucrose per 1 g of the active ingredient sodium phenylbutyrate. This should be taken into account if you have diabetes. If you have been told by the doctor that you have an intolerance to some sugars, refer to the doctor before taking the medicine.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the medicine dosage and treatment regimen.

Dosage

The dosage and treatment regimen will be determined by the doctor only. The daily dose will be determined based on your body weight or body surface, and will be adjusted according to your protein tolerance and diet.

You will need to routinely perform blood tests to determine your daily dose. The doctor will tell you the amount of granules you should take.

Do not exceed the recommended dose.

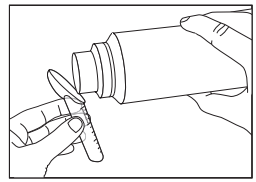
Method of administration

Pheburane is a medicine taken by mouth. Since the granules dissolve slowly, Pheburane should not be administered through a feeding tube that goes through the abdomen to the stomach (gastrostomy) or through a feeding tube that goes through the nose to the stomach (nasogastric tube).

Pheburane must be taken with a special protein-reduced diet.

Take Pheburane with each meal or feeding. In small children, this can be 4 to 6 times per day. The doses of the medicine prescribed for you by the doctor are expressed in grams of sodium phenylbutyrate.

A calibrated measuring spoon which dispenses up to 3 g sodium phenylbutyrate is provided with the package.



Use this spoon only to measure out the dose. Do not use this measuring spoon with any other medicine.

To measure the dose:

- The lines on the measuring spoon indicate the amount of Pheburane in grams of sodium phenylbutyrate. Take the correct amount as prescribed for you by the doctor.
- Pour the granules directly into the spoon as shown in the picture above.
- Tap the spoon once on the table to give a horizontal level of granules in the spoon and continue filling the measuring spoon, if necessary.

The granules can be directly swallowed with a drink (water, fruit juice, protein-free infant formula) or sprinkled on to a spoonful of solid foods (mashed potatoes or apple sauce).

If you mix the granules with food, it is important that you take it immediately. This will keep the granules from producing any taste.

You will need to take this medicine and to follow a diet throughout your life.

If you accidentally took a higher dosage

Patients who took very high doses of sodium phenylbutyrate experienced:

- Sleepiness, tiredness, light-headedness and confusion (less frequent).
- Headache.
- Changes in taste (taste disturbances).
- Decrease in hearing.
- Disorientation.
- Impaired memory.
- Worsening of existing neurological conditions.

If you experience any of these symptoms, you should immediately contact your doctor or the nearest hospital emergency room for supportive treatment.

If a child has accidentally swallowed the medicine, refer immediately to your doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.

If you forget to take the medicine

If you forgot to take this medicine at the required time, take the next dose as soon as possible, with the next meal, but make sure that there are at least 3 hours between two doses. Do not take a double dose to compensate for the forgotten dose.

Adhere to the treatment as recommended by the doctor.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them.

If you have any further questions regarding use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Pheburane may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

If persistent vomiting occurs, contact your doctor immediately.

Very common side effects (may occur in more than 1 in 10 people)

Irregular menstrual periods and stopping of menstrual periods in women of child-bearing age.

If you are sexually active and your period stops altogether, do not assume that this is caused by Pheburane. If this happens, consult with your doctor, since the absence of menstrual period may be caused by pregnancy (see "Pregnancy and breastfeeding" section) or by menopause.

Common side effects (may occur in more than 1 in 100 people)

Changes in number of blood cells (red blood cells, white blood cells and platelets), changes in the amount of bicarbonate in the blood, reduced appetite, depression, irritability, headache, fainting, fluid retention (swelling), changes in taste (taste disorder), stomachache, vomiting, nausea, constipation, abnormal skin odor, rash, abnormal kidney function, weight gain, altered laboratory tests values.

Uncommon side effects (may affect more than 1 in 1000 people)

Deficiency in red blood cells due to failure of the bone marrow, bruising, altered heart rhythm, rectal bleeding, stomach inflammation, stomach ulcer, inflammation of the pancreas.

If a side effect occurs, if one of the side effects worsens or if you are suffering from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (Exp. Date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions

Store in the original package.

Do not store at a temperature above 25°C.

After the first opening, can be used for up to 45 days.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Sugar spheres 250-355, hypromellose, ethylcellulose N7, macrogol 1500, povidone K25.

What the medicine looks like and the contents of the package:

White to cream-colored granules.

The granules are packaged in a plastic bottle with a child-resistant cover and a desiccant. The bottle contains 174 g granules.

Each package contains 1 bottle. A calibrated measuring spoon is provided.

Manufacturer and address: Eurocept International B.V., Ankeveen, Netherlands.

Registration holder and address: Truemed Ltd., 10 Beni Gaon St., Poleg Industrial Park P.O Box 8105, South Netanya, Israel.

This leaflet was revised in December 2021 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 153-57-34275.

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