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

The medicine is dispensed with a doctor's prescription only

Sapropterin Teva
Soluble tablets

The active ingredient:
Each soluble tablet contains:
Sapropterin dihydrochloride 100 mg
(equivalent to 77 mg of sapropterin)
For information regarding inactive ingredients, see in section 2 – "Important information about some of the ingredients of the medicine" and section 6 – "Additional information".
Read the entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine. If you have additional 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.

1. WHAT IS THE MEDICINE INTENDED FOR?

Sapropterin Teva is intended for the treatment of adults and children of all ages, in cases of accumulation of high levels of the amino acid phenylalanine in the blood, a condition which can be harmful. These conditions are called: hyperphenylalaninemia (HPA) or phenylketonuria (PKU). Sapropterin Teva decreases these levels in patients who respond to BH4, making it possible to increase the amount of phenylalanine in the diet of these patients.
Sapropterin Teva is also intended for treatment in cases of an inherited disease called BH4 deficiency in adults and children of all ages, in which the body is unable to produce enough BH4. Because of low levels of BH4, phenylalanine is not used properly, the level of phenylalanine increases and the accumulation of phenylalanine causes harm. The administration of sapropterin, which replaces the BH4 that the body cannot produce, reduces the excess of phenylalanine in the blood and makes it possible to increase the tolerance to phenylalanine in the diet.
Therapeutic class:
Sapropterin Teva belongs to a group of preparations that are basic substances for metabolism in the body.
Sapropterin Teva contains an active ingredient which is a synthetic copy of a natural substance found in the body called tetrahydrobiopterin (BH4).
The substance BH4 is required in the body to use the amino acid phenylalanine in order to create another amino acid called tyrosine.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to sapropterin or to any of the other ingredients this medicine contains (see section 6 – "Additional information").

Special warnings regarding the use of the medicine
Before treatment with Sapropterin Teva, inform the doctor if:
- You are 65 years of age or older.
- You have kidney or liver problems.
- You are ill. It is recommended to consult the doctor, because during an illness, the levels of phenylalanine in the blood may increase.
- You have a tendency for convulsions.

During the treatment with sapropterin, your doctor will recommend tests to determine the levels of phenylalanine and tyrosine in the blood, in order to adjust your treatment dosage of sapropterin or to adjust your diet.
You should follow the diet recommended to you by the doctor. Do not change your diet without consulting the doctor.
Even if you are taking sapropterin, if the levels of phenylalanine in the blood are not properly controlled, you may develop severe neurological problems. The doctor will continue to monitor the levels of phenylalanine in your blood frequently during the treatment with sapropterin, **to make sure that the levels of phenylalanine are not too low or too high.**
Drug interactions
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:
- Levodopa, for the treatment of Parkinson's disease.
- Medicines to treat cancer (such as: methotrexate).
- Medicines for treatment of bacterial infections (such as: trimethoprim).
- Preparations that cause blood vessels to dilate (such as: glyceryl trinitrate (GTN), isosorbide dinitrate (ISDN), sodium nitroprusside (SNP), molsidomin and minoxidil).

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you are pregnant or are planning to become pregnant, consult your doctor or pharmacist before using the medicine.
If you are pregnant, your doctor will explain to you how to properly control the levels of phenylalanine. If these levels are not closely controlled before and when you become pregnant, this may harm you and your baby.
The first choice of treatment is a medically supervised diet that limits the absorption of phenylalanine before and during pregnancy. Your doctor will consider treatment with sapropterin if strictly adhering to this diet is not sufficient to reduce the levels of phenylalanine in the blood.
Do not use this medicine if you are breastfeeding.
Driving and operating machinery
Sapropterin is not expected to affect the ability to drive or operate machinery.
Important information about some of the ingredients of the medicine
This medicine contains less than 1 mmol (23 mg) of sodium per tablet, and is therefore considered "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation.
The dosage and treatment regimen will be determined only by the doctor.
Dosage
Phenylketonuria (PKU)
The accepted starting dose in adults and children is 10 mg for each kg of body weight. The dose of soluble tablet(s) should be taken as a single dose with a meal, to increase the level of absorption. The dose should be taken at the same time every day, preferably in the morning.
Your doctor may adjust your dose to 5-20 mg for each kg of body weight per day, depending on your condition.
BH4 deficiency
The accepted starting dose in adults and children is 2-5 mg for each kg of body weight. The medicine should be taken with a meal to increase the absorption.
Divide the total dose into 2-3 doses, taken during the day.
The doctor may adjust your dose up to 20 mg for each kg of body weight, depending on your condition.
The following table is an example of how the appropriate dose is calculated:

Body weight (kg)	Number of tablets (a dose of 10 mg/kg)	Number of tablets (a dose of 20 mg/kg)
10	1	2
20	2	4
30	3	6
40	4	8
50	5	10

Do not exceed the recommended dose.
Method of use
For PKU patients, the total daily dosage is taken once a day at the same time, preferably in the morning.
For patients with BH4 deficiency, the total daily dosage is divided into 2-3 doses per day.
Use in all patients
Place the number of tablets prescribed for you in a glass of water as described below and stir until dissolved.
It may take several minutes for Sapropterin Teva to dissolve. If you want to accelerate the dissolving process, the tablet can be crushed. You may notice particles in the solution, but they do not alter the effectiveness of the medicine.
You should drink the sapropterin solution together with a meal within 15-20 minutes of when you started to prepare it.
Do not swallow the desiccant in the bottle.
Use in patients who weigh more than 20 kg
Dissolve the tablet(s) in a glass with 120-240 ml of water and stir until dissolved.
Use in children who weigh up to 20 kg
The dose of Sapropterin Teva is based on body weight, and will change as your child grows. The doctor will instruct you regarding:
- The number of Sapropterin Teva tablets required for one dose.
- The amount of water required to mix one dose of Sapropterin Teva.
- The amount of solution you need to give your child in order to administer the prescribed dose.

Your child should drink the Sapropterin Teva solution with a meal, at the same time each day, preferably in the morning.
Give the solution to your child within 15-20 minutes of its preparation. If it is not possible to give the dose within 15-20 minutes after dissolving the tablets, discard the medicine in the trash. You will need to prepare a new solution since the solution must not be used after 20 minutes.
The supplies required to prepare and give your child a dose of Sapropterin Teva
- The number of Sapropterin Teva tablets required for one dose
- A measuring cup with graduations of 20, 40, 60 and 80 ml
- A glass
- A small teaspoon or a clean utensil for mixing
- An oral syringe with graduations of 1 ml (a 10 ml syringe for administering volumes of up to 10 ml or a 20 ml syringe for administering volumes above 10 ml)

Ask the doctor for a measuring cup to dissolve the tablets and for 10 ml or 20 ml oral syringes if you do not have these supplies.
Steps for preparing and taking the dose:
- Place the number of tablets prescribed for your child in the measuring cup. Pour the amount of water into the measuring cup according to the doctor's instructions (for example: the doctor has told you to use 20 ml to dissolve one tablet of Sapropterin Teva). Make sure the amount of liquid matches the amount instructed by the doctor. Stir with a small teaspoon or with a clean utensil until the tablets dissolve.
- If the doctor has told you to give only part of the solution, put the tip of the oral syringe in the measuring cup. Pull the plunger slowly to draw the amount instructed by the doctor.
- Transfer the solution to a glass by pushing the plunger slowly until all of the solution in the syringe has been transferred to the glass for administration (for example: if the doctor has told you to dissolve 2 tablets of Sapropterin Teva in 40 ml water and to give your child 30 ml, you should use the 20 ml oral syringe twice to draw 30 ml (that is, 20 ml + 10 ml) of Sapropterin Teva solution and transfer it to the glass for administration). Use a 10 ml oral syringe for administering volumes of up to 10 ml or a 20 ml oral syringe for administering volumes above 10 ml.
- If your child is too young to drink from a glass, you can give the Sapropterin Teva solution using the oral syringe. Draw the volume prescribed from the prepared solution in the measuring cup and place the tip of the syringe inside the baby's mouth. Push the plunger slowly, a small amount at a time, until all of the solution in the syringe is administered.
- Discard what remains of the solution. Remove the plunger from the oral syringe. Wash both parts of the syringe and the measuring cup with warm water and allow to air dry. When the oral syringe is dry, put the plunger back in the syringe. Store the syringe and the cup for the next use.

If you accidentally took a higher dosage
If you accidentally took a higher dosage, call your doctor or pharmacist immediately. You may feel side effects including headache and dizziness. If you took an overdose or a child accidentally swallowed this medicine, go to the doctor or to a hospital emergency room immediately and take the package of the medicine with you.
If you forgot to take the medicine
Do not take a double dose to make up for the missed dose. Take the next dose at the usual time.
If you stop using the medicine
Even if there is an improvement in your health, do not stop treatment without prior consultation with your doctor, since the levels of phenylalanine in your blood may increase.
If you have any other questions regarding use of the preparation, consult your doctor or pharmacist.
How can you contribute to the success of the treatment?
Follow the treatment as recommended by the doctor.
Do not take medicines in the dark! Check the label and the dose every time you take a medicine. Wear glasses if you need them.

4. SIDE EFFECTS

As with any medicine, using Sapropterin Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects, you may not experience any of them.
Refer to a doctor immediately:
Few cases of allergic reactions (such as skin rash and serious reactions) have been reported. Their frequency is unknown (frequency cannot be estimated from the available data).
If raised, red and itchy areas (hives) appear on the skin, or if you have a runny nose, fast or irregular heartbeat, swelling of the tongue and throat, sneezing, wheezing while breathing, severe breathing difficulties or dizziness, you may be having a serious allergic reaction to the medicine. If you notice these signs, refer to the doctor immediately.
Other side effects:
Very common side effects (effects that occur in more than 1 patient out of 10 patients):
Headache and rhinitis.
Common side effects (effects that occur in up to 1 out of 10 patients):
Sore throat, nasal congestion or stuffy nose, cough, diarrhea, vomiting, abdominal pain, too low levels of phenylalanine in blood tests, indigestion, nausea.
Side effects of unknown frequency (the frequency cannot be estimated from the available data):
Gastritis (inflammation of the lining of the stomach), esophagitis (inflammation of the lining of the esophagus).
If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult the doctor.
Reporting side effects
Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link:
https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- **Store at a temperature below 25°C.**
- **Keep in the original package to protect from humidity and light.**
- The desiccant should be left inside the bottle, and the bottle should be closed tightly after each use.
- Do not discard medicines via the wastewater system or household waste. Ask your pharmacist how to discard medicines you no longer use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, the medicine also contains:
Mannitol, pregelatinised starch, crospovidone, sodium stearyl fumarate, ascorbic acid, riboflavin.
What does the medicine look like and what are the contents of the package?
Sapropterin Teva are slightly mottled, off-white to light yellow, round, soluble tablets. One side of the tablet is debossed with "L71" and the other side is debossed with "T".
Sapropterin Teva is marketed in packages of 30 or 120 soluble tablets. The bottle contains a desiccant.
Not all package sizes may be marketed.
Name and address of the manufacturer and license holder:
Teva Israel Ltd.
124 Dvora HaNevi'a St., Tel Aviv 6944020
The leaflet was revised in December 2024.
Registration number of the medicine in the national drug registry of the Ministry of Health: 177.96.37322.

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