

Package leaflet: Information for the user

Sapropterin Dihydrochloride 100 mg soluble tablets sapropterin dihydrochloride

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Sapropterin Dihydrochloride is and what it is used for
2. What you need to know before you take Sapropterin Dihydrochloride
3. How to take Sapropterin Dihydrochloride
4. Possible side effects
5. How to store Sapropterin Dihydrochloride
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1. What Sapropterin Dihydrochloride is and what it is used for

Sapropterin Dihydrochloride contains the active substance sapropterin which is a synthetic copy of a body's own substance called tetrahydrobiopterin (BH4). BH4 is required by the body to use an amino acid called phenylalanine in order to build another amino acid called tyrosine.

Sapropterin Dihydrochloride is used to treat hyperphenylalaninaemia (HPA) or phenylketonuria (PKU) in patients of all ages. HPA and PKU are due to abnormally high levels of phenylalanine in the blood which can be harmful. Sapropterin Dihydrochloride reduces these levels in some patients who respond to BH4 and can help increase the amount of phenylalanine that can be included in the diet.

This medicine is also used to treat an inherited disease called BH4 deficiency in patients of all ages, in which the body cannot produce enough BH4. Because of very low BH4 levels phenylalanine is not used properly and its levels rise, resulting in harmful effects. By replacing the BH4 that the body cannot produce, Sapropterin Dihydrochloride reduces the harmful excess of phenylalanine in the blood and increases the dietary tolerance to phenylalanine.

2. What you need to know before you take Sapropterin Dihydrochloride

Do not take Sapropterin Dihydrochloride

- if you are allergic to sapropterin or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking Sapropterin Dihydrochloride, particularly:

- if you are 65 years of age or older
- if you have problems with your kidney or liver
- if you are ill. Consultation with a physician is recommended during illness as blood phenylalanine levels may increase
- if you have predisposition to convulsions

When you are treated with Sapropterin Dihydrochloride, your doctor will test your blood to verify how much phenylalanine and tyrosine it contains and may decide to adjust the dose of Sapropterin Dihydrochloride or your diet if needed.

You must continue your diet treatment as recommended by your doctor. Do not change your diet without contacting your doctor. Even if you take Sapropterin Dihydrochloride, if your phenylalanine blood levels are not well controlled, you can develop severe neurologic problems. Your doctor should continue to monitor your blood phenylalanine levels often during your treatment with Sapropterin Dihydrochloride, **to make sure that your blood phenylalanine levels are not too high or too low.**

Other medicines and Sapropterin Dihydrochloride

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. In particular you should tell your doctor if you are using:

- levodopa (used to treat Parkinson's disease)
- medicines for treatment of cancer (e.g. methotrexate)
- medicines for treatment of bacterial infections (e.g. trimethoprim)
- medicines that cause dilation of blood vessels, (such as glyceryl trinitrate (GTN), isosorbide dinitrate (ISDN), sodium nitroprusside (SNP), molsidomin, minoxidil).

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

If you are pregnant your doctor will tell you how to control phenylalanine levels adequately. If these are not strictly controlled before or when you become pregnant, this could be harmful to you and to your baby. Your doctor will monitor the restriction of dietary phenylalanine intake prior and during pregnancy.

If the strict diet does not adequately reduce phenylalanine amount in your blood your doctor will consider whether you must take this medicine.

You should not take this medicine if you are breast-feeding.

Driving and using machines

Sapropterin Dihydrochloride is not expected to affect the ability to drive and use machines.

Sapropterin Dihydrochloride contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Sapropterin Dihydrochloride

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Dosing for PKU

The recommended starting dose of Sapropterin Dihydrochloride in patients with PKU is 10 mg for each kg of body weight. Take Sapropterin Dihydrochloride as a single daily dose with a meal to increase the absorption, and at the same time each day, preferably in the morning. Your doctor may adjust your dose, usually between 5 and 20 mg for each kg of body weight per day, depending on your condition.

Dosing for BH4 deficiency

The recommended starting dose of Sapropterin Dihydrochloride in patients with BH4 deficiency is 2 to 5 mg for each kg of body weight. Take Sapropterin Dihydrochloride with a meal to increase the absorption. Divide the total daily dose into 2 or 3 doses, taken over the day. Your doctor may adjust your dose up to 20 mg for each kg of body weight per day, depending on your condition.

The table below is an example of how an appropriate dose is calculated

Body weight (kg)	Number of 100 mg tablets (dose 10 mg/kg)	Number of 100 mg tablets (dose 20 mg/kg)
10	1	2
20	2	4
30	3	6
40	4	8
50	5	10

Method of administration

For PKU patients, the total daily dose is taken once a day at the same time each day, preferably in the morning.

For BH4 deficiency patients, the total daily dose is divided into 2 or 3 doses over the day.

Use in all patients

Place the prescribed number of tablets in a glass or cup of water or apple juice as accurately described below and stir until dissolved.

It may take a few minutes for the tablets to dissolve. To make the tablets dissolve faster you can crush them. Small particles may be visible in the solution, but they will not affect the effectiveness of the medicine.

Drink the dissolved preparation of Sapropterin Dihydrochloride with a meal within 15 to 20 minutes of its preparation.

Sapropterin Dihydrochloride soluble tablets may also be crushed and then mixed in a small amount of soft foods, such as apple sauce or pudding.

If necessary, Sapropterin Dihydrochloride soluble tablets may be administered via enteral feeding tube. For details how to do so, please ask your doctor, pharmacist or nurse.

Use in patients above 20 kg body weight

Place the tablets in a glass or cup (60 to 240 ml) of water or apple juice and stir until dissolved. The soluble tablets may also be stirred in a small amount of soft foods.

Use in children up to 20 kg body weight

The dose is based on body weight. This will change as your child grows. Your doctor will tell you:

- the number of Sapropterin Dihydrochloride tablets needed for one dose
- the amount of water or apple juice needed to mix one dose of Sapropterin Dihydrochloride
- the amount of solution you will need to give your child for their prescribed dose.

Your child should drink the solution with a meal.

Give your child the prescribed amount of solution within 15 to 20 minutes after dissolving. If you are not able to give your child's dose within 15 to 20 minutes after dissolving the tablets, you will need to prepare a new solution as the unused solution should not be used beyond 20 minutes. For dosage equal

to 100 mg and multiples of 100 mg, the soluble tablets may also be mixed in a small amount of soft foods, such as apple sauce or pudding.

Supplies needed to prepare and give your child's dose of Sapropterin Dihydrochloride

- The number of Sapropterin Dihydrochloride tablets needed for one dose
- A medicine cup with graduation markings at 20, 40, 60 and 80 ml
- A glass or cup
- Small spoon or clean utensil for stirring
- Oral syringe (graduated in 1 ml divisions) (10 ml syringe for administration of volumes of ≤ 10 ml or 20 ml syringe for administration of volumes of > 10 ml)

Ask your doctor for the medicine cup for dissolving the tablets and the 10 ml or 20 ml oral syringe if you do not have these supplies.

Steps for preparing and taking your dose:

- Place the prescribed number of tablets in the medicine cup. Pour the amount of water or apple juice into the medicine cup, as instructed by your doctor (e.g. your doctor told you to use 20 ml for dissolving one Sapropterin Dihydrochloride tablet). Check to make sure that the amount of liquid lines up with the amount that your doctor tells you. Stir with the small spoon or clean utensil until the tablets dissolve.
- If your doctor told you to administer only a portion of the solution, point the tip of the oral syringe into the medicine cup. Slowly pull back the plunger to withdraw the amount as instructed by your doctor.
- Transfer the solution by pushing on the plunger slowly until all of the solution in the oral syringe is transferred to a glass or cup for administration (e.g. if your doctor told you to dissolve two Sapropterin Dihydrochloride tablets in 40 ml water or apple juice and administer 30 ml to your child, you would have to use the 20 ml oral syringe two times to draw up 30 ml (e.g. 20 ml + 10 ml) of the solution and transfer it to a glass or cup for administration). Use a 10 ml oral syringe for administration of volumes ≤ 10 ml or a 20 ml oral syringe for administration of volumes > 10 ml.
- If your baby is too small to drink from a glass or a cup you may administer the solution via the oral syringe. Draw up the prescribed volume from the solution prepared in the medicine cup and place the tip of the oral syringe into your baby's mouth. Point the tip of the oral syringe towards either cheek. Push on the plunger slowly, a small amount at a time, until all of the solution in the oral syringe is given.
- Throw away any remaining solution. Remove the plunger from the barrel of the oral syringe. Wash both parts of the oral syringe and the medicine cup with warm water and air dry. When the oral syringe is dry, put the plunger back into the barrel. Store the oral syringe and the medicine cup for next use.

If you take more Sapropterin Dihydrochloride than you should

If you take more Sapropterin Dihydrochloride than prescribed, you may experience side effects that could include headache and dizziness. Immediately contact your doctor or pharmacist if you take more Sapropterin Dihydrochloride than prescribed.

If you forget to take Sapropterin Dihydrochloride

Do not take a double dose to make up for a forgotten dose. Take the next dose at the usual time.

If you stop taking Sapropterin Dihydrochloride

Do not stop taking Sapropterin Dihydrochloride without prior discussion with your doctor, as phenylalanine levels in your blood may increase.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Few cases of allergic reactions (such as skin rash and serious reactions) have been reported. Their frequency is not known (frequency cannot be estimated from the available data).

If you have red, itchy, raised areas (hives), runny nose, fast or uneven pulse, swelling of your tongue and throat, sneezing, wheezing, serious difficulty in breathing or dizziness, you may be having a serious allergic reaction to the medicine. If you notice these signs, contact your doctor immediately.

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

Headache and runny nose.

Common side effects (may affect up to 1 in 10 people)

Sore throat, nasal congestion or stuffy nose, cough, diarrhoea, vomiting, stomach ache, too low levels of phenylalanine in blood tests, indigestion and feeling sick (nausea) (see section 2: “Warnings and precautions”).

Not known side effects (frequency cannot be estimated from the available data)

Gastritis (inflammation of the lining of the stomach), oesophagitis (inflammation of the lining of the gullet).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Sapropterin Dihydrochloride

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton after “EXP”. The expiry date refers to the last day of that month.

This medicinal product does not require any special temperature storage conditions. Keep the bottle tightly closed in order to protect from moisture.

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. Contents of the pack and other information

What Sapropterin Dihydrochloride contains

- The active substance is sapropterin dihydrochloride. Each tablet contains 100 mg of sapropterin dihydrochloride equivalent to 77 mg of sapropterin.
- The other ingredients are mannitol (E421), crospovidone type A, copovidone K28, ascorbic acid (E300), sodium stearyl fumarate, riboflavin (E101), anhydrous colloidal silica (E551). See section 2. “Sapropterin Dihydrochloride contains sodium”.

What Sapropterin Dihydrochloride looks like and contents of the pack

Sapropterin Dihydrochloride 100 mg soluble tablets are off-white to light yellow, approximately 10 mm x 3.65 mm, round tablet debossed with “11” on one side and breakline on the other side. The score line is not intended for breaking the tablet.

It is available in bottles with child-resistant closure with screw cap containing desiccant (silica). Each bottle contains 30 or 120 soluble tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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Other sources of information

Detailed information on this medicine is available on the Medicines and Healthcare Products Regulatory Agency web site: <http://www.mhra.gov.uk>.