

Merck Serono

MERCK

# Kuvan® 100 mg soluble tablets

Sapropterin dihydrochloride

Read all of this leaflet carefully before you start taking this medicine.

- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

**In this leaflet:**

1. What Kuvan is and what it is used for
2. Before you take Kuvan
3. How to take Kuvan

**1. WHAT KUVAN IS AND WHAT IT IS USED FOR**

Kuvan 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.

Kuvan is used for the treatment of hyperphenylalaninaemia (HPA) or phenylketonuria (PKU), due to abnormally high levels of phenylalanine in the blood, which can be harmful. Kuvan 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.

Kuvan is also used for the treatment of an inherited disease called BH4 deficiency, 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, Kuvan reduces the harmful excess of phenylalanine in the blood and increases the dietary tolerance to phenylalanine.

**2. BEFORE YOU TAKE KUVAN**

**Do not take Kuvan**

If you are allergic (hypersensitive) to sapropterin or any of the other ingredients of Kuvan.

**Take special care with Kuvan**

You should consult your doctor:

- if your child that was prescribed Kuvan is under 4 years of age
- 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
- if you are using any of the medicines listed below under "Taking other medicines"

When you are treated with Kuvan, your doctor will test your blood to verify how much phenylalanine and tyrosine it contains and may decide to adjust the dose of Kuvan 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.

**Taking other medicines**

You should consult your doctor if you are taking:

- levodopa (used to treat Parkinson's disease)
- inhibitors of dihydrofolate reductase (e.g. methotrexate, trimethoprim)
- agents that cause vasodilation, including those administered topically, by affecting nitric oxide (NO) metabolism or action, including the classical NO donors (such as glyceryl trinitrate (GTN), isosorbide dinitrate (ISDN), sodium nitroprusside (SNP) and molsidomin), phosphodiesterase type 5 (PDE-5) inhibitors and minoxidil.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

**Taking Kuvan with food and drink**

Kuvan should be taken with food at the same time each day preferably in the morning.

**Pregnancy and breast-feeding**

For Kuvan no information is available for human pregnancies.

**4. Possible side effects**

**5. How to store Kuvan**

**6. Further information**

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, birth or postnatal development.

If maternal phenylalanine levels are not strictly controlled before and during pregnancy, this could be harmful to the mother and the foetus. In case of pregnancy your doctor will tell you how to control phenylalanine levels adequately. Physician-supervised restriction of dietary phenylalanine intake prior to and throughout pregnancy is the first choice of treatment in this patient group. The use of Kuvan should be considered only if strict dietary management does not adequately reduce blood phenylalanine levels.

Be sure to tell your doctor if you are pregnant or breast-feeding, if you think you might be pregnant, or if you are planning to become pregnant or are planning to begin breast-feeding.

You should not take Kuvan if you are breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicine.

**Driving and using machines**

No studies on the effects on the ability to drive and use machines have been performed. Kuvan is not expected to affect the ability to drive and use machines.

**3. HOW TO TAKE KUVAN**

Always take Kuvan exactly as your doctor has told you. You should check with your doctor if you are not sure.

**Dosage**

**PKU**

The usual starting dose of Kuvan in adult and paediatric patients with PKU is 10 mg for each kg of body weight. Take the soluble tablets 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.

**BH4 deficiency**

The usual starting dose of Kuvan in adult and paediatric patients with BH4 deficiency is 2 to 5 mg for each kg of body weight. Take the soluble tablets 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 up to 20 mg for each kg of body weight per day, depending on your condition. It may be necessary to divide the total daily dose into 2 or 3 doses, distributed over the day, to achieve the best therapeutic effect.

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

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

**Method of Administration**

**Use in adults**

Place the tablets in a glass or cup (120 to 240 ml) of water and stir until dissolved.

#### Use in children

The prescribed number of tablets should be placed in a glass or cup (up to 120 ml) of water and stir until dissolved.

For doses below 100 mg, one tablet should be dissolved in 100 ml of water. Your doctor will tell you to administer only a certain volume of the solution corresponding to the appropriate dose. An accurate measuring device with suitable graduations should be used for this purpose.

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 Kuvan with a meal, at the same time each day, preferably in the morning within 15 to 20 minutes of its preparation.

Make sure you do not swallow the desiccant capsule contained in the bottle.

#### If you take more Kuvan than you should

If you take more Kuvan than prescribed, you may experience side effects that could include headache and dizziness. You should immediately contact your doctor or pharmacist if you take more Kuvan than prescribed.

#### If you forget to take Kuvan

Do not take a double dose to make up for a forgotten dose.

#### If you stop taking Kuvan

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

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

#### 4. POSSIBLE SIDE EFFECTS

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

Frequencies of side effects are defined as:

- very common: affects more than 1 user in 10
- common: affects 1 to 10 users in 100
- uncommon: affects 1 to 10 users in 1,000
- rare: affects 1 to 10 users in 10,000
- very rare: affects less than 1 user in 10,000
- not known: frequency cannot be estimated from the available data.

**Very common side effects:** headache and runny nose.

**Common side effects:** sore throat, nasal congestion or stuffy nose, cough, diarrhoea, vomiting, stomach ache and too low levels of phenylalanine in blood tests.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

#### 5. HOW TO STORE KUVAN

Keep out of the reach and sight of children.

Do not use Kuvan 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.

Store below 25°C.

Keep the bottle tightly closed in order to protect from moisture.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

#### 6. FURTHER INFORMATION

##### What Kuvan 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), calcium hydrogen phosphate anhydrous, crospovidone type A, ascorbic acid (E300), sodium stearyl fumarate, and riboflavin (E101).

##### What Kuvan looks like and contents of the pack

Kuvan is supplied as soluble tablets. The soluble tablets are off-white to light yellow and have "177" imprinted on one face.

It may be available in bottles with child resistant closure of 30, 120 or 240 soluble tablets. Each bottle contains a small plastic tube of desiccant (silica gel). Not all pack sizes may be marketed.

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Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu/>. There are also links to other websites about rare diseases and treatments.