



(sapropterin dihydrochloride)
Tablets or Powder for Oral Solution



What are KUVAN® (sapropterin dihydrochloride) Tablets for Oral Use and Powder for Oral Solution?

KUVAN is a form of the cofactor (or helper) BH4 that already naturally exists in your body. In people who respond to treatment with KUVAN, it works in the body just like BH4 does to help stimulate residual PAH enzyme activity to convert Phe to tyrosine and lower blood Phe levels. KUVAN has been prescribed along with a low-Phe diet to lower blood Phe levels in many people with PKU of all ages and types—even classic!



KUVAN Facts

- Scientists around the world have studied the safety of BH4, the active ingredient in KUVAN, for over **30** years.
- The safety of KUVAN Tablets has been tested in over **600** people with PKU of all ages in BioMarin clinical trials.
 - During the clinical trials, the most common side effects reported were: headache, diarrhea, abdominal or throat pain, upper respiratory tract infections, vomiting and nausea. These same side effects were seen in patients taking placebo (sugar pill) tablets.
- BioMarin maintains patient registries of over **1,000** patients that collects data related to the safety of KUVAN.
- Over **7,100** people with PKU have been treated with KUVAN Tablets in the United States since its FDA approval in 2007.

Phenylketonuria (PKU) is caused by a defect in an enzyme called phenylalanine hydroxylase (PAH). The PAH enzyme uses tetrahydrobiopterin (BH4), a naturally occurring cofactor (or helper) in the body, to break down phenylalanine (Phe) into tyrosine. Tyrosine is a building block for many proteins and important chemicals called neurotransmitters that help brain function which can influence the way someone feels, thinks, and acts.

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In PKU, the PAH enzyme is not working properly and is unable to break down Phe in your body. When tyrosine is not produced and Phe builds up in the blood, it can cause a variety of signs and symptoms, including mental, behavioral, neurological, and physical problems.

Could KUVAN be right for you?

Talk with your doctor and together, *You* can decide!

Indication

KUVAN® (sapropterin dihydrochloride) Tablets for Oral Use and Powder for Oral Solution are approved to reduce blood Phe levels in people with a certain type of Phenylketonuria (PKU). KUVAN is to be used with a Phe-restricted diet.

Important Safety Information

It is not possible to know if KUVAN will work for you without a trial of the medicine. Your doctor will check your blood Phe levels when you start taking KUVAN to see if the medicine is working.

Starting KUVAN does not eliminate the need for ongoing dietary management. Any change to your diet may impact your blood Phe level. Follow your doctor's instructions carefully. Your doctor and dietitian will continue to monitor your diet and blood Phe levels throughout your treatment with KUVAN **to make sure your blood Phe levels are not too high or too low**. If you have a fever, or if you are sick, your Phe level may go up. Tell your doctor and dietitian as soon as possible so they can make any necessary changes to your treatment.

Children younger than 7 years old treated with KUVAN doses of 20 mg/kg per day are at an increased risk for low levels of blood Phe compared with children 7 years and older. Frequent blood monitoring is recommended in this population to ensure that blood Phe levels do not fall too low.

Tell your doctor if you have ever had liver or kidney problems, have poor nutrition or have a loss of appetite, are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed.

KUVAN is a prescription medicine and should not be taken by people who are allergic to any of its ingredients. KUVAN and other medicines may interact with each other. Tell your doctor about **all the medicines you take**, including prescription and over-the-counter medicines, vitamins, herbal and dietary supplements.

If you forget to take your dose of KUVAN, take it as soon as you remember that day. Do not take 2 doses in a day. If you take too much KUVAN, call your doctor for advice.

The most common side effects reported when using KUVAN are headache, runny nose and nasal congestion, sore throat, diarrhea, vomiting, and cough. Additional adverse reactions reported in connection with worldwide marketing include sore throat, heartburn or pain in the esophagus, inflammation of the lining of the stomach, indigestion, stomach pain, and nausea. These are not all the possible side effects seen with KUVAN. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1.800.FDA.1088.

KUVAN can cause serious side effects, including:

- **Severe allergic reactions.** Stop taking KUVAN and **get medical help right away** if you develop any of these symptoms or a severe allergic reaction:
 - Wheezing or trouble breathing
 - Nausea
 - Flushing
 - Lightheadedness or fainting
 - Coughing
 - Rash
- **Inflammation of the lining of the stomach (gastritis).** Gastritis can happen with KUVAN and may be severe. **Call your doctor right away if you experience:**
 - Severe upper stomach-area discomfort or pain
 - Blood in your vomit or stool
 - Nausea and vomiting
 - Black, tarry stools
- **Too much or constant activity (hyperactivity) can happen with KUVAN.** Tell your doctor if you experience hyperactivity, including fidgeting, moving around or talking too much.

For more information, call BioMarin RareConnections™ at 1.866.906.6100.

Please read the attached Full Patient Information.

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