

What is PKU?

PKU (phenylketonuria) is an inherited metabolic disorder caused by a deficiency of the enzyme phenylalanine hydroxylase (PAH).

This enzyme is required for the breakdown of phenylalanine (Phe), an amino acid found in most foods including meat, eggs, dairy products, whole grains and many fruits and vegetables. Without sufficient activity of PAH, Phe accumulates to abnormally high levels in the blood and tissues which can be toxic to the brain. The consequences of sustained high Phe levels may include a variety of serious neurological complications, including mental retardation and brain damage, mental illness, seizures, tremors, and cognitive and behavioral problems.

There are an estimated 50,000 people in the developed world with PKU. Each year an average of 325 babies are born with the disease in the U.S. All newborns in the U.S. are tested for PKU before discharged from the hospital.

Managing PKU With Diet Alone Poses Many Challenges

To maintain non-toxic blood Phe levels, individuals with PKU must adhere to a severely restricted life-long diet consisting of supplemental medical foods and foods that are low in Phe. For many, however, maintaining a Phe-restricted diet is extremely challenging, especially during adolescence. As a result, phe levels in many PKU patients remain high, which may cause problems with neurocognitive functioning.

Kuvan, the First and Only Treatment for PKU, Can Help Lower Blood Phe Levels



KUVAN® (sapropterin hydrochloride) Tablets is the first and only FDA-approved medication for PKU. This treatment reduces blood Phe levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4-) responsive PKU. Kuvan is a pharmaceutical formulation of BH4, the natural cofactor for the PAH enzyme, which stimulates activity of the residual PAH enzyme to metabolize Phe into tyrosine. Kuvan is to be used in conjunction with a Phe-restricted diet.

Please see reverse for full indication and important safety information.

More Hope on the Way: Second PKU Drug Now in the Pipeline

Currently, BioMarin's second product candidate for PKU is under evaluation in human clinical trials. PEG-PAL (PEGylated recombinant phenylalanine ammonia lyase), an injectable enzyme substitution therapy, may have the potential to treat the entire spectrum of patients with low, moderate to severe PKU.

Resources

BPPS (BioMarin Patient and Physician Support program)
BioMarin is committed to assisting patients with PKU obtain access to Kuvan through the BPPS program.
Contact: 1-877-MY-KUVAN (1-877-695-8826)
or online at: bpps@bmrn.com.

www.pku.com

www.kuvan.com

www.bmrn.com

Kuvan® is a registered trademark of BioMarin Pharmaceutical Inc. Kuvan has received orphan drug status in both the United States and European Union. PEG-PAL has received orphan drug status in the United States.

Full Indication and Important Safety Information

KUVAN® (sapropterin dihydrochloride) Tablets is approved to reduce blood Phe levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria (PKU). KUVAN is to be used with a Phe-restricted diet.

Important Safety Information

High blood Phe levels are toxic to the brain and can lead to lower intelligence and decrease in the ability to focus, remember and organize information. Any change you make 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.

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 see if they have to adjust your treatment to help keep your blood Phe levels in the desired range.

KUVAN is a prescription medicine and should not be taken by people who are allergic to any of its ingredients. Tell your doctor if you have ever had liver or kidney problems, are nursing or pregnant or may become pregnant, have poor nutrition or are anorexic. Your doctor will decide if KUVAN is right for you. Tell your doctor about all the medicines you take.

The most common side effects reported when using KUVAN are headache, diarrhea, abdominal pain, upper respiratory tract infection (like a cold), throat pain, vomiting, and nausea.

To report SUSPECTED ADVERSE REACTIONS, contact BioMarin Pharmaceutical Inc. at 1-866-906-6100, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

To learn more, please visit www.kuvan.com for full prescribing information. If you have any questions about this information, please talk with your doctor.