

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) is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalanemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

Prolonged exposure to elevated blood Phe levels in PKU patients can result in severe neurologic damage. The initiation of Kuvan therapy does not eliminate the need for careful monitoring of blood Phe levels and ongoing dietary management.¹

Some patients receiving Kuvan can experience significant drops in blood Phe levels. Patients should be monitored closely to ensure that blood Phe levels do not fall too low.¹

Not all patients with PKU respond to treatment with Kuvan. Response to treatment can only be determined by a therapeutic trial of Kuvan.¹

Kuvan has not been studied in patients with liver or renal impairment. Patients who have these conditions should be carefully monitored when receiving Kuvan. Caution should be used with the administration of Kuvan to patients who are receiving levodopa and drugs that affect nitric oxide-mediated vasorelaxation or folate metabolism.¹

The most serious adverse reactions reported during Kuvan administration (regardless of relationship to treatment) were gastritis, spinal cord injury, streptococcal infection, testicular carcinoma, and urinary tract infection. Mild to moderate neutropenia was also noted. The most common adverse reactions were headache, diarrhea, abdominal pain, upper respiratory tract infection, pharyngolaryngeal pain, vomiting, and nausea.¹