

The **KUVAN** Response Test

A Patient's Guide



An educational brochure brought to you by BioMarin Pharmaceutical Inc.

KUVAN[®]
(sapropterin dihydrochloride) Tablets

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.

Please read the enclosed Patient Information.


(sapropterin dihydrochloride) Tablets

Congratulations!

You, your doctor and your **PKU Clinic Team** have made an important decision to see if you respond to **KUVAN**. Before you get started there is some **important information** for you and your family to review and steps you can take to ensure your test for response is as accurate as possible.



KUVAN was well studied in PKU patients

The health risks of not treating PKU are very high.

Staying safe and healthy can be a challenge with PKU. You must make smart choices in what your child eats and drinks. Making smart and safe choices in medicine is just as important.

BH4 has been used to treat PKU since the early 1990s.

In addition, the active ingredient in KUVAN, BH4, has been studied for 30 years in infants, children, and adults with PKU and other conditions.

The safety of KUVAN has been confirmed in multiple studies. In these studies, patients treated with KUVAN had about the same rate of side effects as patients who were treated with a placebo (a pill without any medicine in it).

The most common side effects reported were:

- Headache
- Diarrhea
- Abdominal (stomach) pain
- Throat pain
- Upper respiratory tract infections (like a cold)
- Vomiting and nausea

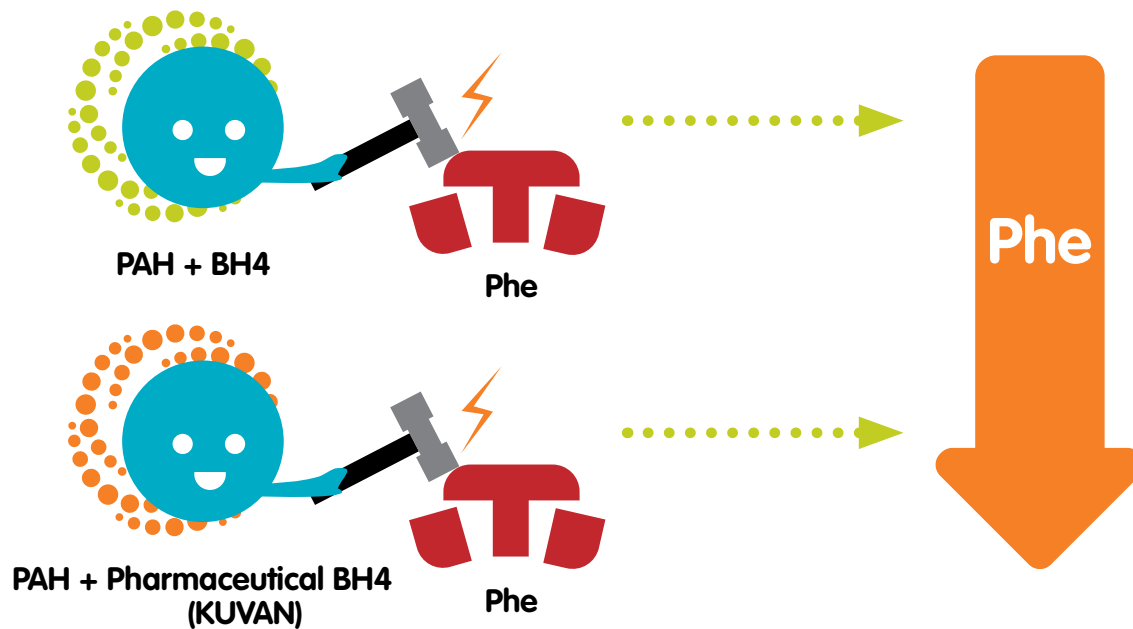
Similar rate of
side effects in
clinical trials

KUVAN

Placebo

KUVAN is a pharmaceutical form of natural BH4

KUVAN works like natural BH4



BH4 is a natural substance found in the body. It helps reduce **Phe** to safe levels in the blood. The active ingredient in KUVAN is a synthetic version of BH4. It works the same way, by helping the **PAH** enzyme “wake up” and process Phe. This helps keep Phe levels in the blood low.

Seeing if KUVAN will work for you

The following are steps you can expect your doctor and PKU Clinic to discuss with you when preparing for your KUVAN test for response. The test for response will be individually tailored to you so it is important to always follow the directions given to you by your doctor or PKU Clinic.

When preparing for your KUVAN test for response you will be asked to:

- Perform and submit a baseline blood test.
- Complete and submit a baseline diet record.
- Make sure you have enough medical food to maintain a consistent diet during the test for response.
- **Not make any lifestyle or diet changes** while you are being tested for a response, unless directed by a Health Care Provider.
- Take KUVAN once a day at the same time of day, with food.

Preparation Notes

Prepare for success!

The KUVAN test for response takes about 4 weeks and during that time it will be important for you to do all you can to ensure an accurate test. Below are some tips to consider:

- Make sure you have enough medical food on hand.
- Ensure you have what you need to collect and submit your blood spots. Remember, test the same time each day and by the same method.
- Be sure to **keep your lifestyle and diet consistent** during the Test for Response. This is not a good time to change your diet, exercise routine or your general lifestyle.
- If you are sick or become sick during your test for response, talk to your doctor immediately to determine if you should continue or re-try your test.
- Discuss any questions with your clinician.

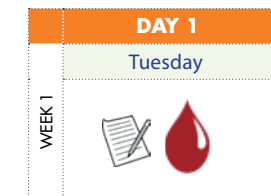
Preparation Notes

My KUVAN Test for Response

The space provided below is for you, your doctor and PKU Clinic Team to outline your personal need to take KUVAN, draw blood or complete a Diet Record. Put a sticker on the day to show

KUVAN test for response. Use a pen to note the days when you completed the task.

Sample Calendar Entry



| | DAY 1 | DAY 2 | DAY 3 | DAY 4 | DAY 5 | DAY 6 | DAY 7 |
|--------|-------|-------|-------|-------|-------|-------|-------|
| WEEK 1 | | | | | | | |
| WEEK 2 | | | | | | | |
| WEEK 3 | | | | | | | |
| WEEK 4 | | | | | | | |
| WEEK 5 | | | | | | | |
| WEEK 6 | | | | | | | |

Day of Week
i.e. Friday

Notes:

of KUVAN Tablets per day: _____

Allowable Phe from foods: _____

Formula prescription: _____

STICKERS KEY



3-Day Diet Record Entry



Take KUVAN (with food)



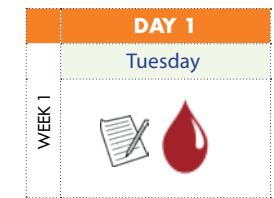
Take Blood Phe Level

My KUVAN Calendar

Continue to place stickers as you continue your treatment on KUVAN.

This will help you stay on track and get into a routine.

Sample Calendar Entry



| | DAY 1 | DAY 2 | DAY 3 | DAY 4 | DAY 5 | DAY 6 | DAY 7 |
|--------|-------|-------|-------|-------|-------|-------|-------|
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3-Day Diet Record Entry



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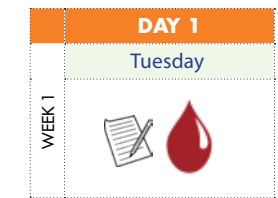
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3-Day Diet Record Entry



Take KUVAN (with food)



Take Blood Phe Level



Extra help for living with PKU

Please see important safety information on page 2, and read the enclosed patient package insert.

Talk to your doctor or dietitian to see if KUVAN is right for you.

Learn more about KUVAN by visiting www.KUVAN.com,
www.PKU.com, or by calling **1-877-MY-KUVAN (1-877-695-8826)**.

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