KUVAN®
(sapropterin dihydrochloride)
Tablets or Powder for Oral Solution

PKU Discussion Guide

# PKU can have a major impact on a person's well-being, leading to trouble with brain function and a cycle of decline[1]

Consistently engaging PKU patients on topics involving their day-to-day lifestyle can help to reveal the unseen symptoms they may be experiencing, yet may be unaware of.

In fact, it's not uncommon for those closest to a patient to recognize the signs and symptoms of high or unstable blood Phe levels more often than the patient themselves.

The ACMG Guidelines for PKU state that individuals returning to therapy can see an improvement in many of the symptoms associated with high or unstable blood Phe levels.

Consistently asking the right questions can help you uncover if a patient is struggling to manage their blood Phe levels and their PKU.

**This is a guide to help you navigate into a deeper dialogue with patients and have more honest conversations about their PKU management.**

## 1 Symptoms

***Do you have a hard time completing tasks? Does anyone ask you if you're feeling a bit "off"?***

- ☐ Do you find yourself having trouble staying focused or feeling "foggy"?
- ☐ Are you having trouble remembering things lately? Or does it take a little longer for things to sink in?
- ☐ How has your memory been lately? Are you feeling more forgetful or absent-minded?
- ☐ Are you feeling any symptoms of sadness, anxiety, or depression? If so, can you give me some examples?

## 2 Planning

***Have you recently changed anything in the way you manage your PKU?***

- [ ] How do you manage your PKU? Walk me through the routines or habits you have developed around meal times, or when taking treatment or formula.
- [ ] Have you had to change or cheat on your diet during events like vacations, holidays, or work gatherings? How did this make you feel?
- [ ] Tell me about a time when you had to go to an event where food was served that you had to avoid. How did it go?

## 3 Relationships

***Who helps you identify symptoms of high blood Phe levels if you experience them?***

- [ ] How are things with your friends and other relationships? Who do you consider a support partner or caregiver who helps you with PKU?
- [ ] What do you think others close to you would say about your mood or relationships lately?
- [ ] Do you feel comfortable in social situations? Do you enjoy making new friends?
- [ ] If you have a significant other, how is the relationship going? Are they helpful with your PKU management, and can they tell when your blood Phe levels are high?

## 4 Lifestyle & Transitions

***What has changed since our last conversation? Is there anything new or different at school/work/home, any holidays or celebrations?***

- ☐ Have you experienced any social pressures related to your PKU? Have there been any instances where your diet prevented you from engaging with other people?
- ☐ Tell me about a time when it was difficult to manage your PKU, and why you think that was.
- ☐ Are you finding it difficult to process information quickly? Do you feel it's hard to keep up in group conversations or when people speak to you?

## 5 KUVAN® (sapropterin dihydrochloride) Tablets or Powder for Oral Solution

***Have you had a trial of or been prescribed KUVAN Tablets or Powder for Oral Solution?***

- ☐ Have you ever missed a dose or forgotten to take your KUVAN?
- ☐ Why do you think that happened, and what did you do? Can you walk me through it?
- ☐ What helps you to remember to take your KUVAN? Do you have a routine or habit that helps you to remember?
- ☐ How do you feel about your KUVAN treatment? Are you experiencing any side effects?

**Please see next page for Important Safety Information.**

## Indication

KUVAN® (sapropterin dihydrochloride) Tablets for Oral Use and Powder for Oral Solution are approved to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria (PKU). KUVAN is to be used in conjunction with a Phe-restricted diet.

## Important Safety Information

Treatment with KUVAN should be directed by physicians knowledgeable in the management of PKU. Prolonged exposure to elevated blood Phe levels in PKU patients can result in severe neurologic damage. Treat all patients with a Phe-restricted diet. The initiation of KUVAN therapy does not eliminate the need for careful monitoring of blood Phe levels and ongoing dietary management to ensure adequate Phe control and nutritional balance. Not all patients with PKU respond to treatment with KUVAN. Response to treatment can only be determined by a therapeutic trial of KUVAN.

KUVAN is not recommended in patients with a history of anaphylaxis to KUVAN. Hypersensitivity reactions, including anaphylaxis and rash have occurred. Discontinue KUVAN treatment in patients who experience anaphylaxis and initiate appropriate medical treatment. Continue dietary Phe restrictions in patients who experience anaphylaxis.

During clinical studies, gastritis was reported as a serious adverse reaction. Monitor patients for signs and symptoms of gastritis.

Monitor patients for hyperactivity.

KUVAN has not been studied in patients with liver or renal impairment. Patients who have these conditions should be carefully monitored when receiving KUVAN.

Monitor patients when co-administering KUVAN with medications known to inhibit folate metabolism, or with levodopa. Monitor patients for hypotension when co-administering KUVAN with medications known to affect nitric oxide-mediated vasorelaxation. Due to a potential for KUVAN to inhibit p-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) in the gut at the therapeutic doses, monitor patients for increased systemic exposure when co-administering KUVAN with medications that are BCRP or P-gp substrates.

Frequent blood monitoring is recommended in the pediatric population.

Some patients receiving KUVAN can experience significant drops in blood Phe levels, and 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. All patients should be monitored closely to ensure that blood Phe levels do not fall too low.

Patients should be advised to notify their physicians in cases of overdose.

The most common adverse reactions (incidence ≥4%) were headache, rhinorrhea, pharyngolaryngeal pain, diarrhea, vomiting, cough, and nasal congestion. Additional adverse reactions reported in connection with worldwide marketing include pharyngitis, esophageal pain, gastritis, dyspepsia, abdominal pain, nausea, and rhinitis.

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 attached full Prescribing Information.

**Reference:**

**1.** Gentile JK, Ten Hoedt AE, Bosch AM. *Mol Genet Metab.* 2010;99(suppl 1):S64-S67.

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