BIMDG
British Inherited Metabolic Disease Group

Sapropterin information sheet for Parents / Guardians

Background information:

Sapropterin is a medicine that can be used to help treat Phenylketonuria (PKU). It has been used to help patients with PKU for a number of years and recently the NHS has agreed to fund its use in England for people with PKU who are found to be 'sapropterin-responsive'. Current practice means that centres managing PKU are unlikely to offer sapropterin to those under 2 years of age.

How does sapropterin work?

In the human body, an enzyme called phenylalanine hydroxylase (PAH) normally breaks down phenylalanine (Phe). The enzyme is helped by a natural chemical within the body called BH_4 (long name = tetrahydrobiopterin!). PKU occurs when the PAH enzyme is either missing or is not working properly, leading to a build-up of Phe in the blood and brain. Sapropterin is a medicine that mimics the natural BH_4 and acts as an extra helper for the PAH enzyme. If a patient with PKU has some PAH enzyme working, this extra helper can give it a boost, helping to reduce Phe levels and allow more natural protein (exchanges) in the diet.

Does sapropterin work for everyone with PKU?

No. Sapropterin is expected to work for approximately 1 in 4 individuals (25%) with PKU. Patients who have a low protein tolerance (for example 3 exchanges in their PKU diet) are very unlikely to benefit from sapropterin as they will not have enough working PAH enzyme to be "helped". Patients who can manage more natural protein in their diet (for example 10 exchanges or more) have a much greater chance of benefiting from sapropterin. These individuals are deemed to be 'sapropterin-responsive'.

What difference will sapropterin make?

For most patients, sapropterin will be used to increase the amount of natural protein (exchanges) within the diet. Patients who are currently unable to keep their Phe levels within the target range may also show a positive response to sapropterin if the medicine improves their Phe control significantly. Your PKU clinical team will agree clear goals with you before starting response testing, whether the aim is to increase protein exchanges or regain control of Phe levels. Sapropterin can also be used to help manage Phe levels in pregnancy – adolescents and young women may consider response testing so they have all the information to help them plan future pregnancies.

Are there any side effects of the drug?

Sapropterin is a well-tolerated drug with a good safety profile and side effects are uncommon. The most common side effects are headache, runny nose and nasal congestion, sore throat and stomach upset. For more information, please discuss with your PKU team.

How do you take sapropterin?

The prescribed number of tablets are dissolved in water or apple juice and must be drunk within 15 minutes with a meal. Sapropterin should be taken at the same time each day usually with breakfast.

How will I know if my child is responsive to sapropterin?

Before using sapropterin regularly, it is necessary to test whether or not a patient is responsive to sapropterin. This is done by completing a trial of responsiveness (see diagram below). To allow long-term treatment, the response test must demonstrate that when using sapropterin a patient:

- can at least double their protein exchanges **OR**
- can regain control of Phe levels (from <50% within target range to >75% within target range)

If a patient does not fulfil either of these criteria, treatment with sapropterin will not be continued. A genetic test may be recommended by the PKU team before response testing. This can help understand whether a patient is likely to respond and, in some cases, will clearly identify that a patient will not respond.

What are the important things to understand about response testing?

After the initial discussion (and result of genetic testing if undertaken), patients opting to proceed will be invited to a clinic appointment to plan the response test. This will include a dietetic assessment, height and weight measurements. Up to date information on exchanges and free foods will be given and counting and measuring phenylalanine exchanges will be reviewed. You will also be asked to complete a food diary for your child at home and return to your dietitian for analysis.

At this appointment the PKU team will also discuss the important steps that patients/families will be required to take in order to complete the response test. These include:

- Sending weekly blood spot samples as requested. There will be a period of a few weeks during which more frequent (up to daily) blood spots will be required. All bloodspots should be taken before breakfast and before any protein substitute is taken.
- Completing food diaries as requested.
- Maximising dietary protein intake under the supervision of the metabolic dietitians prior to introduction of sapropterin.

The PKU team will support you / your child by:

- Providing information as needed
- Reporting all Phe levels and advising accordingly
- Reviewing results of the response test at different stages and deciding if sapropterin is suitable for your child.

Important points to remember:

- Sending bloodspots at the correct times and being very careful to follow your dietitian's advice is essential for the response test to be accurate.
- Only patients who show a genuine response (see diagram below) will be able to continue taking sapropterin.

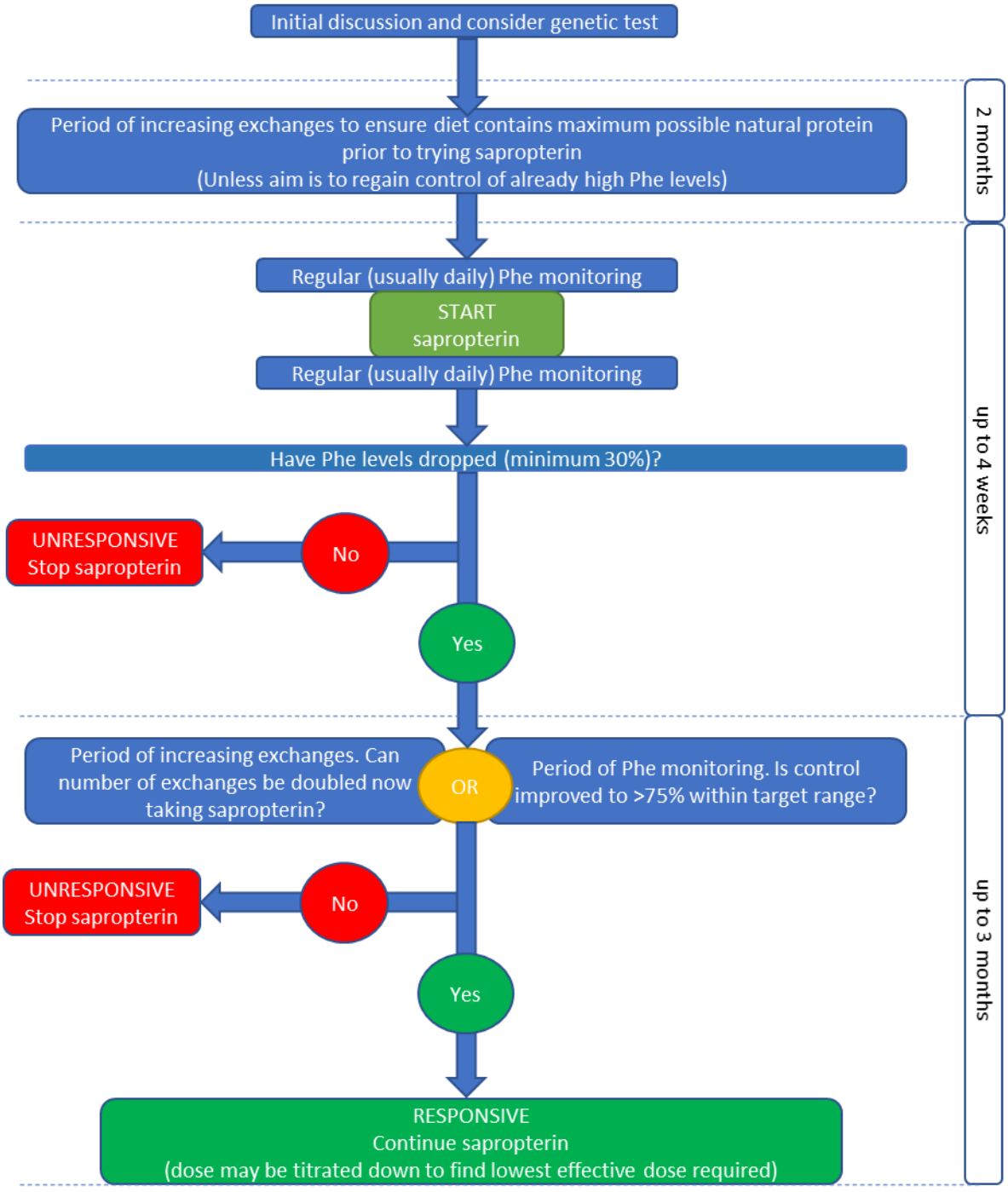
How long will my child be able to take sapropterin?

Patients will no longer be prescribed sapropterin if:

1) They choose to discontinue it for any reason, or

2) It is clear they are no longer getting benefit from it, or

3) They are unwilling to adhere to the requested long-term monitoring requirements.



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