Guidance for appropriate prescribing for phenylketonuria (PKU)

Background

Phenylketonuria (PKU) is an inherited metabolic disorder affecting the metabolism of foods containing protein. In people with PKU, the enzyme, phenylalanine hydroxylase, required to convert the amino acid phenylalanine into tyrosine is either absent or deficient. PKU is diagnosed by screening at birth.

If untreated, the build-up of phenylalanine in the blood can result in severe brain damage. PKU can be successfully treated by a low phenylalanine diet.[1]

Foods that are naturally low in phenylalanine are not restricted in a low phenylalanine diet. These foods include fruits, some vegetables, fats and oils, and sugar. A daily allowance of phenylalanine is permitted made up of 50mg phenylalanine exchanges (equating to approximately 1g protein) from foods such as potatoes, breakfast cereals, some vegetables, and certain manufactured foods. However, as the amount tolerated is only small the daily quantity is usually equivalent to 4-6g of natural protein.

The extremely limited number of the naturally low phenylalanine foods available to PKU patients means that they need supplementation with special low protein foods in order to meet daily energy requirements, add bulk to their diet and increase variety. They will also need a protein substitute that contains all essential amino acids except phenylalanine. Many protein substitutes also contain vitamins and minerals, but a separate supplement of vitamins and minerals may also be needed. In addition to these, milk replacements and glucose polymer supplements are usually necessary, and this is determined by the patient's dietitian.

In England, for the 12 months Aug 22- July 23, over £17 million is spent on metabolic formula specifically for PKU with a further £2.4 million on low-protein foods. For Norfolk & Waveney ICS for the same period the spend is over £274K on metabolic formula and £50K on low protein foods.[2]

Prescribing for these patients can be complex and requires regular review to ensure ongoing appropriateness for the patient's dietary needs.

Recommendations

- Ensure that the patient is being prescribed low protein foods for an ACBS indication i.e. inherited metabolic disorders, renal or liver failure requiring a low protein diet.[3]
- Ensure that the patient has been assessed by a dietitian and find out whether it was decided that they should continue on a low protein diet.
- Ensure that dietitian reviews the patient's low protein diet every six months.
- Review quantities of low protein foods being prescribed to ensure appropriateness based on the maximum number of food units per month, as well as the age of the patient. Prescribing should neither be excessive nor insufficient for the patient's individual needs.
- Ensure prescribing of protein substitutes are in line with recommendations by the patient's dietitian. Review instructions for use and ensure patients take them at least 3 times daily with meals.
- Ensure that quantities and dosages of milk replacements (e.g. Calogen®, Duocal®, Loprofin Drink®, ProZero®, Lattis® and Loprofin Sno-Pro®) and glucose polymer supplements are as recommended by the patient's dietitian.
- Sapropterin (Kuvan®) now has the NICE Technology Appraisal – TA729. This is NHSE funded, and the suppliers are the Trusts via a Patient Access Scheme for the recommended indications. There should be no prescribing in Primary Care via FP10.[4]

The following are included in a PKU diet. As PKU is an ACBS indication, they can be prescribed for PKU patients:

1. Low protein special foods
2. Protein substitutes
3. Vitamins and minerals
4. Milk replacements and glucose polymer supplements

It is recommended that patients have a maximum number of food units per month for all **low protein foods** depending on the age of the patient.

NSPKU suggested quantities for low protein items (2020)[5]

Age of patient with PKU	**Recommended maximum number of low protein items to prescribe each month**
4 months - 3 years	20 units
4 - 6 years	25 units
7 - 10 years	30 units
11 - 18 years	50 units
Adults	50 units
Pre-pregnancy/pregnancy	50 units

** This excludes low protein milk replacements: Calogen®, Duocal®, Loprofin® drink, Prozero®, Lattis® and Sno-Pro®. It also does not include protein substitutes, e.g. PKU Lophlex LQ®, PKU Anamix Junior®, PKU Gel® or glucose polymer supplements.*

The definition of a unit[5] is given below*:

ACBS food	**Definition of one unit**
Pasta/rice	1 pack (up to 500g)
Pasta or potato pots/pasta in sauce	1 pack (up to 300g)
Flour mix/cake mix	1 packet (up to 500g)
Bread/bread rolls	600g – 800g
Pizza bases/pizza base mixes	1 box (up to 500g)
Crackers/crispbread/mini crackers/ croutons/crostini/savoury snacks	1 pack (up to 200g)
Sausage/burger mixes	1 pack/ box (up to 360g dry powder)
Cheese sauce mix	1 pack (225g dry powder)
Soups	1 box (112g dry powder)
Breakfast cereals/hot breakfasts	1 box or pack (up to 400g)
Egg replacer/egg white replacer	1 tub/ box (up to 500g)

Biscuits	1 packet (up to 200g)
Cakes/breakfast bars/dessert mixes /jelly powder/chocolate spread	1 pack (up to 300g)
Energy bars (Vitabite®, Chocotino®)	1 pack

**The table does not include milk replacements such as Calogen®, Duocal®, Loprofin® drink, Prozero®, Lattis® and Sno-Pro®, or glucose polymer supplements. The amount prescribed of these products will vary from patient to patient, so will be determined on an individual basis.*

Please note: The above units are intended as a guide only as package size is variable.

Treat Foods

From about one year old the main bulk of the calories in the diet needs to come from the low protein products such as low protein bread, pasta, rice, crackers, cereals. Some other items may seem like luxury items such as sausage and burger mixes, cake mixes, dessert mixes, energy bars, snack pots, and crisps-equivalent called Snax. However, it is vital that children with PKU do not develop a taste for the ordinary versions of these foods, so it is important the parents have low protein alternatives to give in order to aid compliance & assure good phenylalanine control.

Protein substitutes

Protein substitutes should be taken at least 3 times daily with meals in order to keep the phenylalanine levels steady throughout the day, unless otherwise advised by the patient's dietitian. Cost-effective protein substitutes should be used where equivalent products exist.

Review of diet and discontinuation of low protein diet

A low protein diet for PKU is advocated for life although some adult patients choose to come off the diet (strict dietary adherence is recommended through-out pregnancy). Adult PKU patients in Norfolk and Waveney are ideally reviewed once a year. There is no longer an adult outreach clinic at NNUH and so current adult patients have been given the choice of continuing follow up with the St. Thomas's Metabolic Team by travelling to London, or transferring to the Addenbrookes Adult Metabolic Team in Cambridge. All paediatric patients will be transferred to the Addenbrookes Metabolic team at age 16.

Adapted from Telford and Wrekin CCG

References

1. National Society for Phenylketonuria (NSPKU): https://nspku.org/documents/ [Accessed 27.07.2023].
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4. Sapropterin for treating hyperphenylalaninaemia in phenylketonuria. Technology appraisal guidance [TA729] Published: 22 September 2021. https://www.nice.org.uk/guidance/ta729. [Accessed 27.07.23].
5. National Society for Phenylketonuria (NSPKU): The Prescription of Low Protein Foods for Patients with PKU, Sept 2020. https://nspku.org/wp-content/uploads/2020/09/Prescription-Guidelines-NT-Sept-2020.pdf [Accessed 27.07.23].