PKU trio™

A practical guide for the use of **PKU trio™** in young children with phenylketonuria (PKU)

Vitaflo in Association With You

Supporting education in the dietary management of rare diseases

Disclaimer

This practical guide is intended to support the use of PKU trio™ in the dietary management of young children with phenylketonuria (PKU) and should be read in conjunction with local guidelines. This guide is based on American and European guidelines for the management of PKU as well as clinical experience and best practice recommendations for the management of PKU in pediatrics.[1–3]

The guide is intended only for use by healthcare professionals working with patients with PKU.

It is not intended for use by patients with PKU or their families/caregivers.

It provides only general information, and must not be used as a substitute for professional medical advice.

The product information contained within this guide, although accurate at the time of publication, is subject to change.

The most current product information may be obtained by referring to product labels.

Important notice

PKU trio is a medical food for use under medical supervision.

Must only be consumed by people with proven Phenylketonuria under strict medical supervision.

Diet must be supplemented with natural protein, water and other nutrients in prescribed quantities to supply phenylalanine, fluid, and general nutrition requirements.

PKU trio is not a breast milk substitute and is indicated from 1 year of age.

Not for intravenous use.

For enteral use only.

Not for use as a sole source of nutrition.

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Overview

Early childhood can be a particularly difficult time to manage phenylketonuria (PKU) for several reasons. Compared to later in life, phenylalanine (phe) tolerance is more likely to be variable due to rapid growth. Target ranges of serum phe (120–360µmol/L)[1–3] must be maintained, and frequent diet changes may be needed. Additionally, children are exploring different tastes and textures, and may display neophobic responses to food, which are expected aspects of their development.

Despite these challenges, a child with PKU can be given the same opportunities with food introduction as any other child. A variety of tastes and textures (within the protein restriction), should be offered to allow for development of feeding skills such as tongue control, biting, chewing, self-feeding, and social aspects of mealtimes.

As part of this development, solid food begins to replace some of the fluid intake; whether it is breast milk, standard formula, phe-free formula, or a combination. To meet increasing protein requirements as age increases, higher volumes of formula may be required; or formula may need to be concentrated. Avoiding large volumes of phe-free formula, while still meeting protein requirements for growth, encourages appetite and can help with establishing healthy and age-appropriate eating behaviors.

PKU trio is designed to supply protein equivalent (PE) in a volume supporting appropriate feeding development from one year of age and above. This is achieved by a more concentrated formulation than standard phe-free infant formula; supporting progression with the intake of solids.

1.0 Introduction

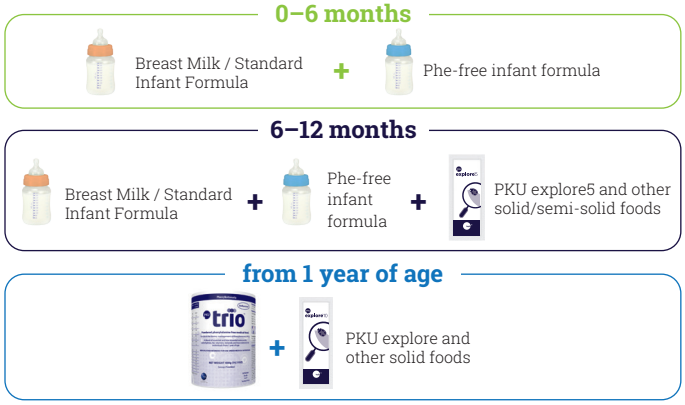
1.1 What is PKU trio?

- A medical food for use in the dietary management of PKU.
- A powdered phenylalanine-free formula providing a trio of macronutrients: protein equivalent (from essential and non-essential amino acids), carbohydrate, and fat.
  - Formulated with DHA and a range of vitamins and minerals.
  - Available in unflavored and vanilla flavor.

1.2 Who may benefit from PKU trio?

- In the transition from phe-free infant formula, from 1 year of age.
- To provide more options for children ages 1 to 3, who need a higher calorie medical food.
- During pregnancy and lactation.

Figure 1. Age appropriate diet transitioning for the PKU infant



Once fully transitioned from phe-free infant formula, **PKU trio** can be used to complement PKU explore if additional volume is needed, helping to meet daily nutrition requirements and preferences.

To learn more about PKU explore™, a semi-solid spoonable medical food for infants 6 months and above, please see the Appendices.

1.3 Nutritional attributes of PKU trio

Calories

- Standard dilution provides 26 kcal/fl oz.
- Provides 405 kcal per 100 g powder or 67 kcal per scoop.

Macronutrients

- Provides 30 g PE per 100 g powder or 5 g PE per scoop.
- Provides carbohydrate and fat to support daily energy requirements.

Fat

- Formulated with a blend of essential fatty acids, linoleic and α-linolenic acid; and the long chain polyunsaturated fatty acid DHA, often deficient in a protein-restricted diet in children.[4, 5]

Micronutrients

- Formulated with a range of micronutrients to help meet daily recommendations.

1.4 Product features

Lower volume

- Supports energy and other nutrition needs from 1 year of age in a smaller volume (more concentrated) than phe-free infant formula.

Flexibility to prepare different concentrations

- **PKU trio** can be consumed at standard dilution (see **Section 3.0 'Preparation Guidelines'**) or concentrated if less volume is preferred. Additional fluid intake may be needed during the day to meet individual fluid requirements.
- The PKU trio calculator is an easy-to-use tool to help individualize PKU formula transition. Please ask your Vitaflo representative about it to learn more.

Figure 2. PKU trio Formula Concentration Guide

	Added PKU trio			Added water	Final volume		
Concentration (calories/ml)	g	scoops	fl oz	ml	fl oz	ml	Osmolality (mOsm/kg)
0.88	44	2 1/2	5 1/2	167	6 1/2	200	860
1.0	49	3	5 1/2	165	6 1/2	200	1040
1.2	59	3 1/2	5 1/2	160	6 1/2	200	1310
1.5	74	4 1/2	5	150	6 1/2	200	1780

*fl oz rounded to the nearest 1/2 fl oz.

Vanilla and **unflavored** options

- The choice of unflavored or vanilla **PKU trio** may help with transitioning from phe-free infant formula.
- Both options can be useful with taste fatigue or poor adherence with the current medical food.
- Easily flavored or used in recipes.*

*Recipe ideas are available upon request from your Vitaflo representative.

2.0 Transitioning to PKU trio

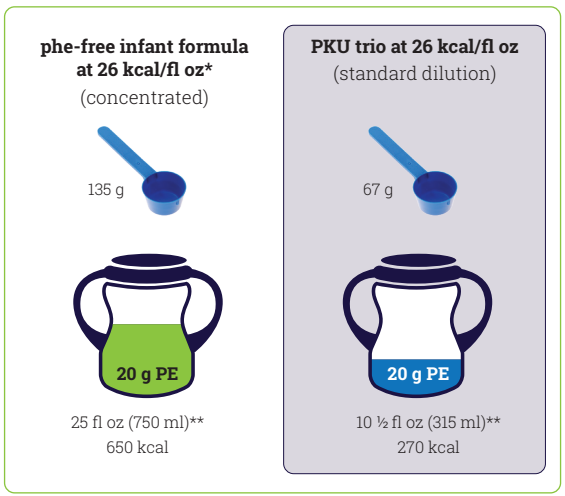
2.1 Overview of transitioning from a phe-free infant formula to PKU trio

Example

As a child reaches 1 year of age, nutritional requirements continue to increase to support growth. The following graphic is for illustrative purposes only and demonstrates the how same PE is achieved in a much smaller volume of PKU trio compared to phe-free infant formula.

1 year old with PKU

Total protein requirements[3]	25 g/day
Energy requirements[6]	850 calories/day
Phe tolerance	250 mg/day (5 g of intact protein)
PE requirements from a medical food	20 g/day



*Volume, powdered formula amount, and calories are based on an average of the available PKU infant formulas on the market.

**Figures rounded.

2.2 Feeding challenges and practical tips

Feeding challenges are common in young children with or without PKU.[7,8] Food refusal is common and this applies to medical foods as well. Taste preferences are established between 4–14 months of age, therefore the timely introduction of PKU trio at 1 year of age may support acceptance.

Tips & tricks for successful feeding

- Aim to establish a routine so the child knows when to expect both **PKU trio** and food. This enables them to better anticipate mealtimes.
- Give **PKU trio** before meals to ensure the entire prescribed volume is taken. It can be helpful if everyone has something to drink at mealtimes so the child does not feel different.
- Present **PKU trio** and food positively. Create a calm, enjoyable mealtime environment without distractions to reduce anxiety around the new medical food.
- Repeat exposure — remember it can take ≥ 8–10 times of offering the same food for a child to become accustomed to the taste and accept it — continue to offer even if it is refused at first.
- Encourage eating with the family and sharing some low protein meals/foods.
- Routine — establish regular meal times, but avoid prolonged feeding. Keep to 20–30 minutes per meal.
- Encourage parent/caregiver to keep a record of intake to help ensure protein prescription is met.

PKU trio tips

- When transitioning from a phe-free infant formula, **PKU trio** unflavored may be preferred as its taste profile is more similar to a first stage medical food.
- Flavoring ideas for PKU trio are available by request from your Vitaflo representative.
- When age-appropriate, children should get involved in the preparation of their medical food as well as other low protein foods, to help them better understand their diet.

2.3 Step-by-step transitioning guide for PKU trio

Transitioning from a phe-free infant formula to **PKU trio** should be attempted at a time and pace that's right for the child and family. Children react differently to change and the transition may be more challenging for some, requiring patience and persistence. Below are the stages of how to successfully transition over to **PKU trio**. In this example **PKU trio** is mixed with the current phe-free formula, however, the two formulas may be given separately.

Based on the same example of the 1 year old child mentioned previously. Receiving:

- 5 g intact protein
- 250 mg phe
- 20 g PE from phe-free infant formula

Tolerance

When transitioning to a new medical food, mild gastrointestinal symptoms, such as constipation or loose stools, may be experienced initially.

If mild intolerance occurs, consider taking a step back and slow the rate of transition until the issue resolves and then continue to progress as tolerated.

Ask your Vitaflo representative about our calculator tool you can use to help with transitioning your patient from their current phe-free formula to PKU trio. The calculator can be used to individualize transition plans, as it includes measurement methods, formula concentration, and number of transition steps.

Start	**Stage 1** Initial introduction of PKU trio	**Stage 2** Advancing volume of PKU trio	**Stage 3** Schedule feeds to accommodate individual needs
PE provided entirely by phe-free infant formula.	Start to replace phe-free infant formula with **PKU trio**. Identify when the child is hungry and most receptive to trying something new. Offer the mixture of phe-free formula at this time, before solids.	Continue to replace the phe-free infant formula with **PKU trio** as tolerated by the child until all feeds are replaced with **PKU trio.**	Feeds can eventually be scheduled to fit more easily into family mealtimes and routine. This also creates time for other developmental activities and play.
5 feeds of phe-free infant formula per day providing 20 g PE per day. 4g PE **x 5 feeds per day**	For all feeds: • Reduce PE from the current phe-free infant formula by a small amount e.g. 2 g PE per feed. • Replace with the volume of **PKU trio** that provides the equivalent PE. 2g PE 2g PE **x 5 feeds per day**	For all feeds: • Continue to increase **PKU trio** while decreasing the phe-free infant formula by volumes equivalent in PE until completely transitioned. 4g PE **x 5 feeds per day**	A reduced overall volume allows for fewer formula feeds throughout the day. 7g PE **x 3 feeds per day**
Fluid requirement likely to be met by phe-free infant formula.	Offer additional fluids after PKU trio and in between feeds to achieve daily fluid recommendations.		
= Phe-free formula for infants = PKU trio	Continue to provide 5 g intact protein/250 mg phe per day. Encourage protein-free and very low protein foods to increase energy from solids. Calories can be added if necessary, by mixing in protein-free foods such as butter/oils.	Phe levels should be consistently within target range before introducing or increasing PKU trio and monitored throughout the transition period according to current standards or practice.	

See '**Section 2.2**' for guidance on incorporating **PKU trio** into mealtimes and addressing feeding challenges.

3.0 Preparation guidelines for PKU trio

The amount of medical food to be consumed daily will be determined by the clinician or dietitian and is dependent upon age, body weight, and medical condition of the individual.

2 level scoops provide 10 g protein equivalent.

Preparation guidelines for PKU trio (standard dilution 26 kcal/fl oz)

Step 1:
Measure 2 level scoops into glass/ mixing cup.

Step 2:
Add approximately 135 ml (4.5 fl oz) of cold water.

Step 3:
Mix well until all of the powder is dissolved.

Step 4:
Drink immediately.

To make more than one serving

If making more than one serving, store prepared formula in a covered container in the refrigerator and use within 24 hours. Re-shake before use.

Storage

Unopened — PKU trio should be stored in a cool dry place.

Once opened — Use within one month.

Household Measurement Guide

Household measurement	Weight of powder (g)	PE (g)	Calories
1 teaspoon	3	1	12
1 tablespoon	9	3	37
1/4 cup	36	11	146
1/2 cup	72	22	292

*All household and scoop measurements are given for a level, unpacked measure taken directly from the can and are approximate.

4.0 Nutrition Information for PKU trio

4.1 Select nutritional information

	per 100 g	per 1 scoop (16.5 g)	per 10 g PE
Calories	405	67	134
Protein equivalent (g)	30	5.0	10
Fat (g)	14.3	2.4	4.8
Docosahexaenoic acid (DHA) (mg)	200	33	66
Total Carbohydrate (g)	38.9	6.4	12.8

For full nutrition profile, visit:

www.VitafloUSA.com

4.2 Protein equivalent (PE), powder weight, scoops and energy chart

PE (g)	Weight of PKU trio (g)	Scoops of PKU trio	Calories
5	16.5	1	67
10	33	2	134
15	49.5	3	201
20	66	4	268
25	82.5	5	335
30	99	6	402
35	115.5	7	469
40	132	8	536
45	148.5	9	603
50	165	10	670

5.0 References

1. van Wegberg, et al. The complete European guidelines on phenylketonuria: diagnosis and treatment. *Orphanet Journal of Rare Diseases*. 2017; 12(1): 162.
2. Acosta PB. *Nutrition Management of Patients with Inherited Metabolic Disorders*: USA Jones & Bartlett Publishers; pp. 119–174.
3. Singh RH, et al. Recommendations for the nutrition management of phenylalanine hydroxylase deficiency. *Genetics in Medicine*. 2014; 16(2): 121–31.
4. Rose, et al. Fat intakes of children with PKU on low phenylalanine diets. *J Hum Nutr Diet*. 2005; 18(5): 395–400.
5. Parra G, et al. Status of nutrients important to brain function in phenylketonuria: a systematic review and meta-analysis. *Orphanet Journal of Rare Diseases* 2018; 13(1): 101.
6. Institute of Medicine (IOM). Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. https://www.nap.edu/catalog/10490/dietary-reference-intakes-for-energy-carbohydrate-fiber-fat-fatty-acids-cholesterol-protein-and-amino-acids.
7. MacDonald A, et al. Abnormal feeding behaviours in phenylketonuria. *J Hum Nutr Diet*. 1997; 10: 163–170.
8. Evans S, et al. Food acceptance and neophobia in children with phenylketonuria: a prospective controlled study. *J Hum Nutr Diet*. 2016; 29(4): 427–433. 12.
9. Acosta PB, Fernhoff PM, Warshaw HS, et al. Zinc and copper status of treated children with phenylketonuria. *JPEN*. 1981; 5(5): 406–9.
10. Barretto JR, Silva LR, Leite ME, Boa-Sorte N, Pimentel H, Purificacao AC, et al. Poor zinc and selenium status in phenylketonuric children and adolescents in Brazil. *Nutr Res*. 2008; 28(3): 208–11.
11. Robert M, Rocha JC, van Rijn M, et al. Micronutrient status in phenylketonuria. *Mol Genet Metab*. 2013; 110 Suppl: S6–17.
12. Rose HJ, White FJ, MacDonald A, Rutherford PJ, Favre E. Fat intakes of children with PKU on low phe diets. *J Hum Nutr Diet*. 2005; 18(5): 395–400.
13. Fekete K, Decsi T. Long-chain polyunsaturated fatty acids in inborn errors of metabolism. *Nutrients*. 2010; 2(9): 965–74.
14. Koletzko B, Lien E, Agostoni C, et. al. The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations. *J Perinat Med*. 2008; 36(1): 5–14.
15. Evans S, et al. Fifteen years of using a second stage protein substitute for weaning in phenylketonuria: a retrospective study. *J Hum Nutr Diet*. 2018; 31(3): 349–356.

6.0 Appendices

6.1 Appendix 1 — What is PKU explore?

PKU explore is a powdered phenylalanine-free medical food, containing a blend of essential and non-essential amino acids, carbohydrate, arachidonic acid (ARA), docosahexaenoic acid (DHA), vitamins and minerals.

It is designed to form a semi-solid (spoonable) consistency when mixed with a small amount of water to support the introduction of solids in the diet of infants from 6 months of age and young children with PKU.

Available in 2 pre-measured packet size options

Product name	Pre-measured packet size	Protein equivalent (PE)	Flavor(s)	Age indication
PKU explore5				
	12.5 g	5 g	unflavored	From 6 months
Mix with 12.5 ml (approx. 1 Tbsp.) of cold water.				
PKU explore10				
	25 g	10 g	orange or raspberry	From 1 year
Mix with 25 ml (1.5–2 Tbsp.) of cold water.				

PKU explore5 unflavored is suitable for introduction from 6 months of age alongside solid foods and PKU explore10 in orange and raspberry options are suitable for introduction from 1 year of age to add flavor variety and support the increasing protein requirements of the child.

6.2 Appendix 2 — Nutritional features of PKU explore

	Units	PKU explore5 (1 packet = 12.5 g of product)	PKU explore10 (1 packet = 25 g of product)
Calories	kcal	43	83
Protein Equivalent	g	5	10
Total Carbohydrate	g	5.2	9.8
Sugars	g	3.5	6.3
Total Fat	g	0.2	0.4
Saturated Fat	g	0.09	0.17
ARA	mg	35	70
DHA	mg	17	35

Micronutrients

10 g PE meets at least 25% of DRI recommendations for micronutrients for ages 7–12 months and 20 g PE from PKU explore meets at least 70% of DRI recommendations for micronutrients for ages 1–3 years.**

A protein-restricted diet increases the risk of micronutrient deficiencies.[9–11] The composition of PKU explore contains a wide range of nutrients including selenium, zinc, iron, calcium, and a comprehensive range of vitamins including vitamin B12 and vitamin D important for nutrition and growth.

Meets RDIs for 16 key micronutrients. For full nutritional information refer to product datasheet, available on **www.VitafloUSA.com

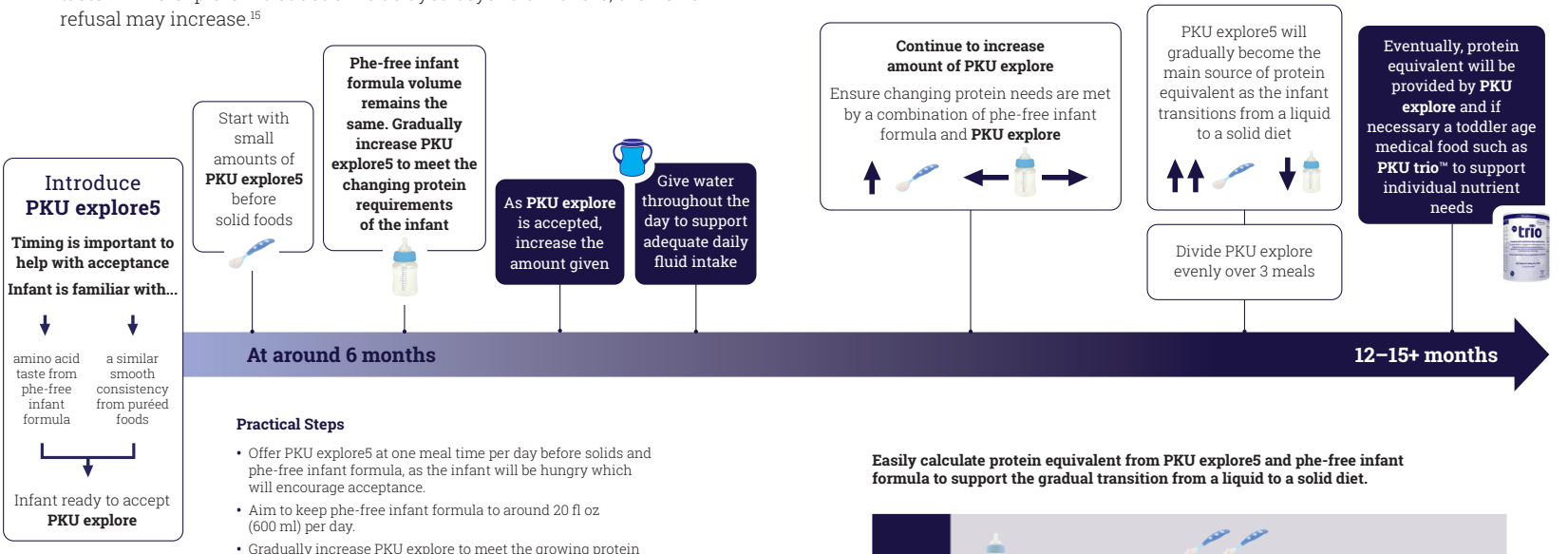
Long Chain Polyunsaturated Fatty Acids (LCPUFAs)

PKU explore is formulated with LCPUFAs, including docosahexaenoic acid (DHA). In the PKU diet, foods rich in LCPUFAs are restricted and therefore intakes are often low. Children on a protein-restricted diet have shown deficiency in DHA.[12–14]

6.3 Appendix 3 — Introduction of PKU explore

Introduce PKU explore5 around 6 months of age

It is important to introduce PKU explore5 before introducing measured portions of protein foods to help the infant become accustomed to its taste. If PKU explore introduction is delayed beyond 6 months, the risk of refusal may increase.[15]



Practical Steps

- Offer PKU explore5 at one meal time per day before solids and phe-free infant formula, as the infant will be hungry which will encourage acceptance.
- Aim to keep phe-free infant formula to around 20 fl oz (600 ml) per day.
- Gradually increase PKU explore to meet the growing protein need with the change in the infants' weight.
- Once the infant consistently takes 5 g PKU Explore5 (2 g PE) at one meal, introduce PKU explore at a 2nd mealtime.
- At 12 months of age PKU explore10 may be introduced for flavor variety and to support protein equivalent intake.

- Phe-free infant formula is important in the 1st year of life. It helps contribute to calorie, fluid and other nutrient needs. However, excessive volumes of phe-free infant formula may interfere with appetite for solid foods.
- Prepare PKU explore5 to the same consistency every time. If this varies widely the infant may reject it due to unfamiliarity.
- Every infant will progress at different rates. Increase PKU explore5 as quickly as the infant accepts and according to protein equivalent needs.

Easily calculate protein equivalent from PKU explore5 and phe-free infant formula to support the gradual transition from a liquid to a solid diet.

~2 g PE	~3 fl oz (90 ml)	OR	5 g PKU explore5 + 1 teaspoon (5 ml) water
~5 g PE	~8 fl oz (240 ml)	OR	1 packet (12.5 g) PKU explore5 + ~1 tablespoon (12.5 ml) water

It is vital that the blood Phe is monitored throughout this process.

Additional Resources

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*Patients who are prescribed select Vitaflo formulas are eligible to enroll in Formula4Success.

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1 year +

PKU explore™10

1 year +

PKU Trio™

3 years +

PKU sphere®15
PKU sphere®20

3 years +

PKU express®15
PKU express®20

3 years +

PKU cooler®10
PKU cooler®15
PKU cooler®20

3 years +

PKU air®20

ALL PRODUCTS ARE FOR USE UNDER MEDICAL SUPERVISION.

A healthcare professional must be consulted to indicate which products are appropriate for the PKU diet.

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