PKU MSUD HCU TYR

explore™

An introduction to complementary feeding and transitioning to a concentrated second stage protein substitute explore™ in infants with an amino acid disorder.

Vitaflo in Association With You

Supporting education in the dietary management of rare diseases

Disclaimer

This practical guide covers an introduction to complementary foods and transitioning to a concentrated low volume spoonable protein substitute (**explore**), in infants diagnosed with an amino acid disorder.

In this guide the following amino acid disorders are considered: **phenylketonuria (PKU), maple syrup urine disease (MSUD), homocystinuria (HCU) and tyrosinaemia (TYR)*.**

All of these amino acid disorders share the same principles of dietary management. Therefore, the management of the introduction to complementary foods and the transitioning to a concentrated protein substitute is considered in one practical guide.

This guide should be read in conjunction with local and national protocols. It is based on best practice over the last 20 years of introducing a concentrated spoonable protein substitute to infants with an amino acid disorder from around six months of age[1].

For organic acidaemias see section 5.3.

The guide **does not cover** the clinical management of these conditions. Refer to section 4.2 for the international management guideline references.

This practical guide is:

- Only to be used by healthcare professionals.
- Not for use by patients or their families/caregivers.
- For guidance only and must not be used as a substitute for professional medical advice or management.

* In this guide we have used the abbreviation TYR to represent tyrosinaemia instead of HT, as Vitaflo uses this within the names of their protein substitutes for tyrosinaemia, e.g. TYR explore5.

Important notice

The **explore** range are foods for special medical purposes (FSMP) for the dietary management of various amino acid disorders - including PKU, MSUD, HCU and TYR (see appendix 5.4 for full **explore** range).

Use under medical supervision.

Not suitable for use as a sole source of nutrition.

Suitable from 6 months to 5 years of age.

For enteral use only.

explore must only be consumed by individuals with a proven amino acid disorder under supervision by the managing clinician or dietitian. Natural protein must be given in prescribed amounts to meet requirements.

Introducing and adjusting explore is based on the individual needs of the child. While practical examples are given in this guide, local practice may vary.

It is the responsibility of the managing healthcare professional to use their clinical judgment to introduce and adjust explore in the most appropriate way for their individual patients.

The product information contained in this guide, although accurate at the time of publication, is subject to change. To ensure accuracy, please refer to product labels or **www.vitafloweb.com**.

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Key to symbols and terms used throughout this practical guide

Symbol	Term	Definition	Precursor amino acid free from
	PKU	Phenylketonuria	Phenylalanine
	MSUD	Maple Syrup Urine Disease	Valine, Isoleucine, Leucine
	HCU	Homocystinuria	Methionine
	TYR	Tyrosinaemia type I, II, III	Tyrosine, Phenylalanine
	PE	Protein Equivalent - the amount of protein provided by a protein substitute. Total protein intake = PE intake from protein substitute + natural protein intake.	
		Breast milk/standard infant formula.	
	Precursor amino acid(s)	This refers to the amino acid(s) that can not be catabolised due to an enzyme defect in metabolic pathway (see table 1 for more detail).	
	**Precursor free amino acid formula for infants**	Precursor free amino acid formula for infants refers to the condition-specific formula for infants free from the appropriate precursor amino acid(s) for the particular disorder being managed.	
	**explore**	**explore** refers to the condition-specific **explore** free from the appropriate precursor amino acid(s) for the management of the particular amino acid disorder.	
	A measured amount of protein	This refers to a measured amount of natural protein from food to provide a prescribed quantity of the relevant precursor amino acid(s). Systems for allocating prescribed amounts of the precursor amino acid(s) vary internationally. In the UK the amino acid is allocated in the form of a daily food exchange system, with different exchange systems for each of the 4 disorders. Some countries use allowance systems, where the individual counts the milligrams of the precursor amino acid(s) they consume as part of their daily allowance. **For the simplicity of this guide, the prescription of precursor amino acid(s) is referred to as a measured amount of protein.**	
	**Very low protein foods**	**Very low protein foods** refer to foods that are very low in protein (precursor amino acid(s)) that can be incorporated into the diet without having a direct impact on target blood amino acid concentrations. Where an 'allowance' system is being used, every mg of precursor amino acid(s) may be counted as part of the patient's daily allowance.	

Practice on calculating measured amounts of protein and very low protein food intake may vary, adhere to local country / international guidelines.

Overview

When complementary foods and a second stage protein substitute are introduced to an infant with an amino acid disorder, feeding can become more complex for both caregivers and healthcare professionals. These changes must not only support the child's developmental and nutritional needs but also maintain satisfactory growth and optimal metabolic control. New tastes are experienced through foods, and breast milk or standard infant formula are gradually replaced by measured amounts of protein containing solids. When choosing an appropriate protein substitute, it is always important to consider the age and developmental stage of the child.

One of the challenges of introducing complementary foods and a second stage protein substitute is to find a balance between giving a variety of very low protein foods and measured amounts of protein, and maintaining sufficient intake of the precursor free protein substitute to meet the infant's requirements. Historically, protein substitutes developed for young children were powders, designed to be reconstituted as liquids. When given to infants aged from 6 months, the high volume of liquid protein substitute may reduce appetite, delaying solid food progression. Administering the second stage protein substitute as a concentrated spoonable semi-solid, encourages appetite and therefore supports introduction of solid foods[1].

Establishing the second stage protein substitute at the right time is essential to ensure it is accepted. Introducing **explore** requires a gradual and progressive approach, increasing the amount according to individual needs. This enables the reduction of precursor free formula for infants, allowing appetite for foods. To support this process, caregivers will need education, ongoing support and practical guidance with clear instructions to help them with the challenges of complementary feeding and establishing the child onto a second stage protein substitute.

Good feeding practices for infants without an amino acid disorder should be followed when possible (see section 5.1). Differences occur with the types of first foods introduced and also the introduction of protein containing foods. To aid the acceptance of solid foods and support long term metabolic control, it is essential that this process is carefully managed[2].

Role of explore

- **Provides a concentrated source of PE and micronutrients, which in the diet for amino acid disorders cannot be provided or are limited due to the restriction of protein rich foods.**
- **Ensures good feeding practice recommendations can be met, by reducing liquid intake and allowing appetite for solid foods to develop[3].**
- **By helping meet infant feeding developmental milestones, explore may reduce potential feeding problems and associated anxiety for both parents/caregivers and the child.**

Vitaflo has developed this practical guide for healthcare professionals on the use and introduction of **explore** for infants at around 6 months of age for either **PKU, MSUD, HCU** or **TYR**. By following the suggested stepwise system for introducing **explore**, it should help establish a suitable framework for protein substitute administration in infants and create a sound foundation for future years.

Contents

1.1 What is explore?

explore is a concentrated powdered protein substitute free from the appropriate precursor amino acid(s)* for the particular disorder, containing essential and non-essential amino acids, carbohydrate, sugar, vitamins, minerals, trace elements, arachidonic acid (ARA) and docosahexaenoic acid (DHA). It is intended for the dietary management of an amino acid disorder from 6 months to 5 years of age.

explore is reconstituted with a small amount of water to form a low volume smooth semi-solid paste that will hold consistency throughout mealtimes. Introducing **explore** from around 6 months of age begins the transition from the precursor free amino acid formula for infants to the concentrated spoonable protein substitute. It is designed to help meet the infant's nutritional and developmental feeding needs; ensuring the goals of the amino acid disorders dietary management are met, aiding growth and metabolic control.

Product Name	Precursor amino acid free from	Premeasured sachet	Protein Equivalent (PE)	Flavour(s)	Age Indication
 **PKU explore5**	Phenylalanine	12.5g	5g	**unflavoured**	From 6 months - ideal for the first stages of complementary feeding
 **PKU explore10**	Phenylalanine	25g	10g	**orange** or **raspberry**	From 1 year - for when complementary feeding is more established and protein requirements increase with weight
 **MSUD explore5**	Valine Isoleucine Leucine	12.5g	5g	**unflavoured**	From 6 months - ideal for the first stages of complementary feed
 **HCU explore5**	Methionine	12.5g	5g	**unflavoured**	From 6 months - ideal for the first stages of complementary feed
 **TYR explore5**	Tyrosine Phenylalanine	12.5g	5g	**unflavoured**	From 6 months - ideal for the first stages of complementary feed

Nutritional Information		explore5 per 12.5g	explore10 per 25g
Energy	kJ	181	351
	kcal	43	83
Fat	g	0.2	0.4
of which saturates	g	0.09	0.17
ARA	mg	35	70
DHA	mg	18	35
Carbohydrate	g	5.3	9.8
of which sugars	g	3.5	6.3
Protein equivalent	g	5.0	10
Free from the appropriate precursor amino acids*	g	-	-

explore contains a wide range of micronutrients, for full nutritional information see **www.vitafloweb.com**

* No added condition specific precursor amino acid(s). They may be present in trace amounts from other ingredients (<10mg/100g powder, <2mg/5g PE sachet, <4mg/10g PE sachet).

1.2 Nutritional features of explore

Protein Equivalent (PE)

Easy to calculate the PE, supporting a staged transition from the precursor free amino acid formula for infants* to the lower volume **explore.**

Volume of precursor free amino acid formula for infants		Protein Equivalent		Volume of explore5
100ml	=	2g	=	5g explore5 + 5ml cold water
250ml	=	5g	=	1 sachet explore5 (12.5g) + 12.5ml cold water
500ml	=	10g	=	2 sachets explore5 (25g) + 25ml cold water

Micronutrients

A protein-restricted diet increases the risk of micronutrient deficiencies[4-6]. The composition of **explore** contains a wide range of micronutrients including selenium, zinc, iron and calcium and a comprehensive range of vitamins including vitamin B12 and vitamin D important for nutrition and growth.

Long Chain Polyunsaturated Fatty Acids (LCPUFAs)

LCPUFA intake is reduced as the rich food sources are restricted in the diet for an amino acid disorder. Children receiving a protein-restricted diet have shown deficiency in docosahexaenoic acid (DHA)[7-8]. **explore** meets requirements for DHA when ≥ 30g PE/day is consumed for infants and young children[9].

explore has an ARA:DHA ratio of 2:1.

* Based on a typical precursor free amino acid formula for infants.

2.1 Overview of the introduction to complementary feeding and explore

The following chart shows an overview of the stepwise practical introduction to complementary feeding, both **very low protein foods** and **measured amounts of protein** from food + **explore**. Details of each step follows in section 2.2.

This is a guide only and every infant will progress at different rates.

Expected progression in feeding development

0–4 months	4–6 months	6–9 months	9–12 months	12–15+ months
 +  **Precusor free amino acid formula for infants**				
• Poor control of head • Swallows liquid	• Sits with support • Can control position of food in mouth • Swallows puréed or strained food	• Begins to sit alone unsupported • Can introduce coarsely mashed food and finger foods • Can drink from a cup	• Sits alone easily • Completes side to side tongue movement • Can take minced/ chopped foods	• Can self feed • Participates in family meals • Stops drinking formula from a bottle • Drinks from a cup

Progressing from breast milk / standard infant formula to complementary foods

Breast milk / standard infant formula

Introducing very low protein foods

Start to introduce tastes of **very low protein foods** first **AFTER** breast milk/standard infant formula + the precursor free amino acid formula for infants.

Gradually increase these foods in quantity, variety and then frequency.

Once accepting **very low protein foods** this signifies readiness to progress to introducing **explore** and **measured amounts of protein**.

Introducing measured amounts of protein

Introduce a **measured amount of protein** to begin to gradually replace breast milk/standard infant formula.

Continue to increase the **measured amounts of protein** to individual tolerance and reduce breast milk/standard infant formula accordingly.

Top up meals with **very low protein foods** to appetite.

Continue to progress texture, introduce finger foods and encourage self feeding.

Total nutritional requirements are met through:

3 chopped/textured meals per day consisting of the allowance of **measured amounts of protein** (to individual tolerance) + **very low protein foods** to appetite + water

+

Divide **explore** evenly over 3 meals.

Give **explore** BEFORE food.

It is important to introduce **explore** BEFORE introducing **measured amounts of protein** to enable the infant to become accustomed to its taste.

Reducing the precursor free amino acid formula for infants and introducing explore

Precursor free amino acid formula for infants

Do not decrease the volume of the precursor free amino acid formula for infants whilst introducing **very low protein food**.

Introducing explore

Start with small amounts to taste.

As **explore** is accepted increase the amount given, decrease the precursor free amino acid formula for infants accordingly.

explore increases throughout the 2nd 6 months of life and beyond to meet growing protein needs.

Maintain volume of precursor free amino acid formula for infants at 500-600ml/day.

Continue transition

Gradually replace the precursor free amino acid formula for infants with **explore**.

Encourage water throughout the day so ensuring fluid requirements are met.

A precursor free amino acid formula for infants is important in the 1st year of life.

Although large volumes should be avoided to allow for developmental progression, continuing a certain amount helps contribute to ensure energy, fluid and other nutrient needs are met.

Appetite and oral intake of food increases throughout this period, which enables energy requirements to be met.

Monitor

- Total protein equivalent
- Weight
- Fluid intake
- Stool pattern (ensure adequate fluid intake)

It is vital that precursor amino acid(s) blood levels are monitored throughout this process.

2.2 Stepwise introduction to complementary feeding

The following chart shows the stepwise practical introduction to complementary feeding, both **very low protein food** and **measured amounts of protein**. In an amino acid disorder introducing complementary food from 17-26 weeks of age can be advantageous, as early exposure to food is likely to lead to acceptance of a wider range of **very low protein foods**, **measured amounts of protein** and **explore**, whilst maintaining blood levels of the precursor amino acid(s) within treatment recommendations[2].

When introducing food, it is best to give **very low protein foods** first as they do not adversely affect blood levels. This allows the infant to experience different tastes without affecting metabolic control. This **promotes a positive feeding experience** as there is less pressure to consume a required amount of food. Once accepting **very low protein foods** this signifies readiness to progress to introducing **explore** and **measured amounts of protein** (exchanges).

From 4 months

Start with 1-2 teaspoons of **very low protein foods**

Food should be a smooth/ semi-solid consistency.

Practical Steps

- Start **very low protein foods** at one mealtime in the day, ideally when the infant is most receptive.
- Initially **very low protein foods** are usually offered **after** breast milk/standard infant formula + the precursor free amino acid formula for infants so it does not affect the volumes consumed.
- Ensure the volume of the precursor free amino acid formula for infants consumed does not reduce whilst introducing **very low protein foods**, but do not increase its volume.

Around 6 months

Increase **very low protein foods** in quantity, variety and then frequency gradually building up to around 8 - 12 teaspoons **after** breast milk/standard infant formula + the precursor free amino acid formula for infants at each meal time.

This signifies readiness to progress to introducing the **explore** and **measured amounts of protein.**

Start to introduce small amounts of **explore** (see section 2.3 for details).

It is important to introduce **explore** before introducing **measured amounts of protein** to enable the infant to become accustomed to its taste.

Encourage drinking from a beaker. Give water throughout the day to ensure an adequate daily fluid intake.

Introduce a **measured amount of protein** to begin to gradually replace breast milk/standard infant formula.

Offer the first **measured amount of protein** at the mealtime the infant is most receptive.

Practical Steps

Teach families how to calculate a **measured amount of protein**.

Example

1g of protein = approx 1 breast feed

1g of protein = 90ml standard infant formula*

- Initially aim for 1 **measured amount of protein** per day.
- Reduce breast milk/standard infant formula accordingly.

One breast feed in combination with the precursor free amino acid formula for infants is likely to provide approximately 1 - 1.5g natural protein, but this amount is determined by the number of breast feeds consumed in 24 hours and the amount of precursor free amino acid formula for infants consumed.

12-15+ months

Gradually introduce more texture and lumpier foods. Introduce a spoon for self feeding.

Continue to increase the **measured amounts of protein** to tolerance and reduce breast milk/ standard infant formula accordingly.

Allow infants to satisfy their appetite by consuming **very low protein foods** to adequately meet their energy needs.

Increase textures to chopped consistency.

Introduce finger foods and encourage self feeding.

The **measured amounts of protein** will:

Eventually completely replace breast milk**/standard infant formula.

Be spread evenly over 3 daily mealtimes.

It usually takes a few weeks to establish **very low protein foods** in the diet but this will vary depending on the developmental readiness of the infant.

Parents should be encouraged to follow the infant's cues of hunger and satiety. Infants should not be forced to eat.

Provide the parent/carer with a suitable list of **measured amounts of protein** foods.

Encourage parent/carer to keep a record of intake as this will help ensure all **measured amounts of protein** are given.

Ensure energy requirements are met, e.g. encourage very low protein cereal, add margarine to vegetables. See section 3.3 for more details.

For more practical tips see section 3.1.

It is vital that precursor amino acid(s) blood levels are monitored throughout this process.

* Check the relevant precursor amino acid(s) content of the standard infant formula being used, there is variation between formulae.

** Breast feeding can continue beyond 12 months as part of precursor amino acid(s) allowance.

2.3 Stepwise introduction to explore

The following chart shows the stepwise introduction to explore.

Around 6 months - introduction to explore

It is important to introduce **explore** before introducing the **measured amounts of protein (exchanges)** to enable the infant to become accustomed to its taste.

If **explore** introduction is delayed beyond 6 months, the risk of refusal may considerably increase[1].

Throughout this process calculate total protein goals and consider natural protein from food. The remaining protein requirements are met by a combination of **explore** and the precursor free amino acid formula for infants, until fully established on **explore**.

Practical Steps

- **explore** is gradually introduced and systematically increased to meet protein requirements unmet by **measured amount of protein** from food and the precursor free amino acid formula for infants.
- Offer **explore** at one meal time per day BEFORE one **measured amount of protein** + the precursor free amino acid formula for infants, as the infant will be hungry which will encourage adherence.
- Once **explore** has been established at one meal time, introduce 5g **explore** (2g PE) at the beginning of each mealtime over the next few weeks.
- Gradually reduce the precursor free amino acid formula for infants to around 500 - 600ml/day, while continuing to increase **explore** to meet protein requirements with the increase in the infant's weight.
- By 12 - 15 months it is expected that most of the precursor free amino acid formula for infants should be replaced by **explore**.
- Divide **explore** evenly over three meals BEFORE **measured amounts of protein** and **very low protein foods** at the same time each day.

Protein equivalent (PE) of explore5 and precursor free amino acid formula for infants*

Volume of precursor free amino acid formula for infants		Protein Equivalent		Volume of explore5
100ml	=	2g	=	5g explore5 + 5ml cold water
250ml	=	5g	=	1 sachet explore5 (12.5g) + 12.5ml cold water
500ml	=	10g	=	2 sachets explore5 (25g) + 25ml cold water

* Based on a typical precursor free amino acid formula for infants.

Introduce explore

to gradually replace the precursor free amino acid formula for infants.

Timing is important

There is a window of opportunity to help promote acceptance.

Infant is familiar with...

- amino acid taste from the precursor free amino acid formula for infants.
- a similar smooth consistency from puréed foods.

Infant ready to accept **explore.**

At around 6 months

12-15+ months

Give water throughout the day to ensure an adequate daily fluid intake.

Start with small amounts of **PKU explore** to taste.

Volume of precursor free amino acid formula for infants remains the same.

As **explore** is accepted increase the amount given.

Reduce the precursor free amino acid formula for infants accordingly.

Continue to increase amount of explore

Ensure changing protein needs are met by a combination of the precursor free amino acid formula for infants and **explore.**

Gradually replace the precursor free amino acid formula for infants with **explore.**

Divide the **explore** evenly over 3 meals.

explore will eventually completely replace the precursor free amino acid formula for infants.

A precursor free amino acid formula for infants is important in the 1st year of life.

Although large volumes should be avoided to allow for developmental progression, continuing a certain amount helps contribute to ensure energy, fluid and other nutrient needs are met.

Appetite and oral intake of food increases throughout this period, which enables energy requirements to be met.

Introduce **explore** at a convenient meal time when the parent/carer is not rushed and the infant is most receptive.

Every infant will progress at different rates, don't hesitate with steps to increase **explore**. Increase **explore** as quickly as the infant accepts and according to protein needs.

For more practical tips see section 3.1.

It is vital that precursor amino acid(s) blood levels are monitored throughout this process.

2.4 Guide for meeting the increasing protein needs of an infant with an amino acid disorder

The following table shows a worked example of how the infant's protein needs are met. It is **only a guide** and every infant will progress at different rates, therefore it may take longer to completely replace the precursor free amino acid formula for infants with **explore**.

Weight	6kg	7kg	8kg	9kg	10kg	11kg	12kg
Approximate age	**Around 6 months** →						**24 months**
Precursor free amino acid formula for infants 	**700ml 14g PE**	**600ml 12g PE**	**600ml 12g PE**	**600ml 12g PE**	**400ml 8g PE**	**200ml 4g PE**	-
Explore 	Start with small amounts of **explore** to taste.	**4g explore x 3 = 5g PE**	**7g explore x 3 = 8g PE**	**9g explore x 3 = 11g PE**	**15g explore x 3 = 18g PE**	**21g explore x 3 = 25g PE**	**27g explore x 3 = 32g PE**
This infant tolerates 4g of natural protein*. Breast milk/ standard infant formula → **Measured amounts of protein** 	**4g protein**	**4g protein**	**4g protein**	**4g protein**	**4g protein**	**4g protein**	**4g protein**
Very low protein food	**Appetite and oral intake of food increases throughout this period, which enables energy requirements to be met.**						
Total protein intake/day	**18g**	**21g**	**24g**	**27g**	**30g**	**33g**	**36g**

The protein requirements in this example are calculated using the UK guideline of 3g total protein/kg/day[10, 11], for infants and children 0 - 2 years old with PKU. In the absence of disorder specific research this guidance for protein intake is used for other amino acid disorders. Local recommendations and policies may differ on protein requirements for these infants and children and should be checked and adhered to where appropriate.

***** Protein tolerance will vary between individuals and between the different conditions.

2.5 Sample meal plan - 10 month old boy with tyrosinaemia

In the table below, a typical meal plan for meeting protein and energy requirements is shown for a child with tyrosinaemia:

Weight of infant	**10kg**
Protein requirements	**30g/day (3g/kg/day[10, 11])**
Natural protein tolerance	**4g**
Amino acid formula for infants	**550ml/day**
TYR explore5	**3 x sachets per day (37.5g powder)**

Remember to give a drink of water at each meal time.

		Protein/PE (g)	kcal
On waking	200ml precursor free amino acid formula for infants 	4	134
Breakfast	1 sachet **TYR explore5**  1 slice of low protein toast, butter and apricot jam  20g yoghurt† + 6 raspberries  150ml precursor free amino acid formula for infants 	**5** 1 3	**43** 123 102
Midday	1 sachet **TYR explore5**  60g sweet potatoes 40g baked beans 5g butter  ½ sachet low protein custard 40g chopped banana 	**5** 2	**43** 169
Evening meal	1 sachet **TYR explore5**  20g low protein pasta 25g spinach Tomatoes /onions  Chopped melon 	**5** 1	**43** 159
Bedtime	200ml precursor free amino acid formula for infants 	4	122
	Total	**30g/day (3g/kg/day)**	**938kcal* (94kcal/kg/day)**

* Calories estimated using manufacturer's labelling, food portion sizes[12] and food composition tables[13].

† Check manufacturer's label.

If infant is still breast feeding, count as part of protein allowance.
Protein tolerance will vary between individuals and between the different conditions.

3.1 Practical points for parents/caregivers for the successful introduction to explore and complementary foods

It is important to share practical advice with parents/caregivers to aid the successful introduction of **explore** and complementary foods. Setting the right foundations and promoting good habits with a consistent approach from the beginning will support success in the long term.

Introducing explore

Be organised - encourage parent/caregiver to be prepared, e.g. **explore** powder pre-measured in a small bowl, baby bib, feeding spoon and water. A small 5ml syringe would be useful for measuring small amounts of water.

Introducing explore - offer the infant **explore** at a time of day when most receptive/interested and a convenient meal time when the parent/carer is not rushed.

Routine - give **explore** at the same time and in the same way each day. Give at the start of each meal or half an hour before to ensure it is taken. Be consistent.

Ensure all of the explore is finished - emphasise the importance of taking the prescribed amount.

Same consistency - if more than one person administers **explore**, ensure that they make it to the same consistency each time. If this varies widely the infant may reject due to unfamiliarity.

Take it slowly and go at the infant's pace - give lots of praise - smiling and encouragement will help the infant accept **explore**. **Persevere** with consistent timings and encouragement.

Offer water - to ensure an adequate daily fluid intake.

Be patient - it is common for any infant to spit out or refuse foods at times. It is no different with **explore**, this is normal infant behaviour. Encourage parents to persevere and keep calm and continue with positive feeding techniques.

During teething - making **explore** up with ice cold water may help with sore gums.

Introducing complementary foods

Encourage the use of **homemade foods** & provide information on suitable commercially available **very low protein foods**.

Provide families with lots of **practical advice** regarding cooking skills and ideas.

Encourage batch cooking, this is especially useful in the early stages when portion sizes are small.

Repeat exposure - remember it can take ≥ 8 times of offering the same food for an infant to become accustomed to the taste and accept it - **continue to offer foods even if at first refused**[14, 15].

Encourage **eating with the family** and share some low protein meals/foods.

Establish **regular meal times**, but **avoid prolonged feeding**, keep to 20 - 30 minutes per meal.

Encourage parent/carer to **keep a record of intake** as this will help ensure all **measured amounts of protein** food are given.

Provide information for other caregivers

Provide any new caregiver with an explanation of the particular amino acid disorder.

Provide the caregiver with clear written instructions of the feeding plan and the necessary feeding equipment.

Emphasise the importance of ensuring the child finishes all of their **explore** at each meal.

3.2 Additional information

Advice on illness

In PKU, HCU and TYR a formal Emergency Regimen (ER) is not normally necessary during illness as acute metabolic decompensation does not occur.

MSUD

It is essential to start an ER at the first sign of illness. This is **not covered** in this guide. It is vital to adhere to international/local country guidelines[16].

For PKU, HCU and TYR

It is normal for an infant to refuse or have difficulties taking their usual amount of **explore** when ill or teething. This may be an anxious time for parents/caregivers and so it is helpful to stay in regular contact with the family to give advice and reassurance and to assess how the infant is progressing. Sometimes parents/caregivers feel that switching protein substitute may help if the child is refusing their protein substitute. This should be avoided and the underlying issues of the illness or teething addressed.

It is very important that an infant continues to take their **explore** during illness to help maintain metabolic control. However it may be necessary to recommend that the infant has the same daily dose, but administered in smaller more frequent amounts throughout the day, e.g. divide into five amounts per day rather than three. More time may be required to administer **explore**.

Continue to offer explore throughout the day even when an infant refuses or is unwell. Giving an infant a 'day off' from their explore will adversely affect their metabolic control and give the wrong message to the infant and family. Stopping explore, even for 24 hours, may create difficulties with its reintroduction.

Extra fluids in the day may be necessary, particularly if the infant has vomiting or diarrhoea.

Parents should be given written advice on how to manage illness and should seek medical advice early.

Feeding problems in toddlers

As with many toddlers, feeding problems are common in young children with amino acid disorders[17, 18]. Although children with an amino acid disorder may be fussy for the same reasons as other children, some issues may be unique to children with specific amino acid disorders, and place them at higher risk of developing feeding problems.

Strategies to minimise or improve feeding problems in an infant with an amino acid disorder

- Good and consistent feeding routines are required from the commencement of complementary feeding and the introduction of **explore**[1].
- Parents/caregivers/families should eat together with the infant to promote a positive environment and social interaction where possible.
- Offer a suitable, healthy and varied low protein diet, but avoid offering too many food choices at one meal.
- Allow infants to satisfy their appetite by consuming **very low protein foods** to adequately meet but not exceed their energy needs. As these foods are **very low protein foods**, they will not adversely affect metabolic control.
- Limit excessive snacking.
- Encourage positive mealtime behaviours e.g. eat at the table together, allow toddler to help set the table.
- The infant should be seated during meals and distractions minimised.
- Encourage self-feeding at the appropriate stage.
- Give **explore** in three equal doses before foods, at the same times each day.

3.3 Meeting energy requirements

When an infant transitions on to a solid diet, energy from breast milk or standard infant formula must be replaced by food. In a child with an amino acid disorder, the transition from an precursor free amino acid formula for infants to a second stage protein substitute such as **explore** creates an energy deficit to allow development of appetite for solid foods.

There has been some concern that the low energy density of a concentrated second stage protein substitute might not compensate for the energy content of the precursor free amino acid formula for infants and this might impact on growth and weight gain.

In an observational study[1] it was found that despite the lower energy content of the complementary feeding protein substitute compared to the precursor free amino acid formula for infants, no infant was reported to have growth issues. It was assumed that an increase in solid food intake compensated for the energy discrepancy. This demonstrated that this type of protein substitute can be introduced without adverse effects on appetite or growth.

A later study looking at the growth, protein and energy intake in children with PKU taking a concentrated weaning protein substitute in the first 2 years of life showed that using the low volume protein substitute met phe-free protein requirements, facilitated transition to solid foods and supported normal growth[19].

It is important to make sure energy demands are met in this transitional period and beyond to facilitate growth and development.

General tips to increase energy intake if needed (section 3.4 for further details):

- Fortify lower energy foods, such as vegetables and fruit, with extra energy, e.g. adding fat
- Offer more energy dense foods rather than increasing portion sizes
- Avoid drinks 1 hour before meals and offer after a meal so the child does not fill themselves up with fluid
- Have mealtimes when the infant is not too tired to encourage cooperation and appetite

explore can be made up with ProZero instead of water to add extra calories. Make up explore in the usual way but add ProZero instead of water. ProZero is a liquid blend of carbohydrate and fat designed as a protein free alternative to milk. It can be used in the dietary management of inborn errors of metabolism from 6 months of age.

3.4 Tips on how to increase energy in the diet

The following methods can be used to increase the energy content of a low protein diet:

Food sources

Low protein	Protein free
Sweet potato Butternut squash Cassava Low protein pasta/rice/flour	Gelatine free jellies Fruit purée Honey (after 1year of age)
TIPS	**TIPS**
These foods are easily incorporated into puddings or savoury dishes: ➢ Cassava to make a low protein crumble ➢ Low protein flours can be used to make cakes/pancakes and dough for bread sticks ➢ Sweet potato and butternut squash in mild curry sauces	Sweet and sugary foods are easily incorporated into puddings or given as snacks: ➢ Add to fruit ➢ Add to low protein pancakes Remember to advise to eat sugary foods within a meal and ensure dental hygiene.

Low protein	Protein free
Mayonnaise* Avocado Low protein cheese*	Cooking oils Margarine Butter Butter spreads Protein free/low protein alternatives to milk*
TIPS	**TIPS**
These foods are easily incorporated into puddings or savoury dishes: ➢ Mix cream* with low protein fruit to make fruit 'ice creams' ➢ Add suitable coconut milk* to low protein vegetable sauces ➢ Mix cream/mayonnaise* with avocado to make a spread for low protein toast	Fats are easily incorporated into savoury meals: ➢ Lightly fry/roast low protein vegetables ➢ Mix into sweet potatoes/butternut squash ➢ Add into low protein tomato based sauces or mild curry sauces

Some of these foods may be counted as part of the protein allowance, depending on the amino acid disorder adhere to local country guidelines.

*** Check manufacturer's label for suitability.**

4.1 General references for the practical guide

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4.2 International management guideline references

General reference

Dixon M, MacDonald A, White F, Stafford J. 17. Disorders of Amino Acid Metabolism, Organic Acidaemias and Urea Cycle Disorders. In: Shaw V (ed.). Clinical Paediatric Dietetics. 4th edition. Oxford, UK: Wiley Blackwell; 2015. p.381-525.

PKU

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MSUD

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HCU

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5.0 Appendices

5.1 Complementary feeding an infant without an amino acid disorder

This summary represents a guide to infant development and common practices for the introduction of complementary foods. Individual infants develop and progress at different rates. Advice should be tailored to the individual infant and nutritional requirements assessed on an individual basis. Complementary feeding practice varies internationally and this should be considered.

	Developmental stage	Recommendations and practice	
Stage 1	**Start -** Introduction of complementary foods begins not before 4 months but no later than 6 months [1 - 4]		
	Infants begin to sit with assistance and develop some head control. Infants begin to mouth, hold and explore objects and may show interest in food. Infants may open their mouth in anticipation of a spoon.	**Homemade or commercial complementary food** Purée texture foods are introduced once per day when the infant is most receptive and progresses to 2-3 times per day according to acceptance. Complementary foods are offered before a milk feed. Common first foods include baby rice, cereals, puréed fruit, puréed vegetables however all food groups, especially iron-rich sources[4, 5] can be offered Foods to avoid include honey, added salt, added sugar[4], rice drinks[6], unpasteurised cheeses and raw shellfish. Foods may be refused initially and it can take more than 8 -10 attempts before being accepted.	**Breast feed/formula** Milk feeds remain the same volume (around 120-150ml/kg/day) and complementary foods are experiential rather than nutritional at this stage. National policy should be consulted regarding recommendations for vitamin and mineral supplementation.
Stage 2	**Progress -** Progression of texture and variety of complementary foods		
	The gag reflex to lumpy foods begins to decline. Infants develop skills to clear a spoon with their top lip. Mouth movements become more coordinated and chewing develops.	**Homemade or commercial complementary food** Frequency of complementary foods progresses to 3 small meals per day, offered before milk feeds. Food consistency can progress according to developmental stage from puréed to lumpy and mashed textures [1]. Once 3 small meals are established, the variety of complementary foods widens to broaden acceptance and exposure.	**Breast feed/formula** A cup or beaker can be introduced from 6 months old. As the quantity of complementary foods increases, the volume of milk feeds reduce according to appetite but should remain at least 500-600mls/day[7]. Water is offered at mealtimes.
Stage 3	**Establish -** Further progression of texture and variety of complementary foods		
	The presence of teeth allows infants to bite harder foods. Motor control develops to enable self-feeding from a spoon.	**Homemade or commercial complementary food** Infants progress to chopped foods, harder finger foods and foods that require more biting and chewing. Snacks are introduced between meals [3]. Variety of foods progresses and is optimised to offer all food groups and nutrients. Mealtimes become more sociable.	**Breast feed/formula** Milk feeds gradually reduce to 2-3 times per day. Water is offered at mealtimes.
Stage 4	**Beyond the first year -** Joining in family meals and self feeding		
	Infants start to recognise foods. Chewing is not fully mature but infants can cope with most textures.	**Family meals** Meals based on foods prepared for the rest of the family/caregivers are offered and social engagement at mealtimes is always encouraged.	**Breast feed/cow's milk/follow-on formula** Continue breast feeds according to mother's/infant's wishes. If formula fed, pasteurized whole cow's milk can replace formula if the complementary feeding diet is adequate to meet nutritional requirements [3] or follow-on formula can be used. Water is offered to meet fluid requirements.

Total nutritional requirements met by 3 chopped meals per day, snacks & drinks from a cup. Protein is achieved from a variety of food sources.

5.2 References for complementary feeding an infant without an amino acid disorder

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5.3 Organic acidaemias

Several countries worldwide undertake expanded new-born screening for some of the organic acidaemias (OAA). Early detection by screening and pre-symptomatic initiation of treatment can greatly improve the outcome.

explore products are also available for the organic acidaemias (i.e.) Methylmalonic Acidaemia (MMA), Propionic Acidaemia (PA) and Glutaric Aciduria Type 1 (GA-I).

For those infants that are able to be introduced to complementary foods and a second stage protein substitute start at the usual time of around 6 months of age. Proceed in a similar method for the management of PKU, MSUD, HCU, TYR that are described in more detail in this guide. The basic principles in the guide to introduce complementary food and the appropriate **explore** can be used, making appropriate adjustments to any calculations or meal plan examples that are discussed.

Although there are similarities between the amino acid disorders and the OAA, there are also differences. The main difference, in relation to protein substitutes, is that, where used, the quantities prescribed tend to be smaller as there is more tolerance of natural protein in OAA.

Some of these patients however never progress onto solids or take very small amounts because of feeding difficulties and so will not be weaned in this way.

To avoid potential confusion, this guide has not focused on the OAA.

For further info on the OAA see references below.

General references for organic acidaemias

Dixon M, MacDonald A, White F, Stafford J. 17. Disorders of Amino Acid Metabolism, Organic Acidaemias and Urea Cycle Disorders. In: Shaw V (ed.). Clinical Paediatric Dietetics. 4th edition. Oxford, UK: Wiley Blackwell; 2015. p.381-525.

MMA/PA

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IVA

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GA Type 1

Boy N, Mühlhausen C, Maier EM, Heringer J, Assmann B, Burgard P, *et al*. Proposed recommendations for diagnosing and managing individuals with glutaric aciduria type I: second revision. Journal of Inherited Metabolic Disease. 2017;40(1):75-101.t

5.4 explore Range

explore is available for the following conditions, suitable from 6 months:

	Product / Condition	Precursor amino acid(s) free from	Flavour	Sachet Size	Protein Equivalent (PE)
	**PKU explore5** Phenylketonuria (PKU)	Phenylalanine	unflavoured	12.5g	5g
	**PKU explore10*** Phenylketonuria (PKU)	Phenylalanine	orange raspberry	25g	10g
	**MSUD explore5** Maple Syrup Urine Disease (MSUD)	Valine Isoleucine Leucine	unflavoured	12.5g	5g
	**HCU explore5** Homocystinuria (HCU)	Methionine	unflavoured	12.5g	5g
	**TYR explore5** Tyrosinaemia (TYR)	Tyrosine Phenylalanine	unflavoured	12.5g	5g
	**MMA/PA explore5** Methylmalonic Acidaemia/Propionic Acidaemia (MMA/PA)	Methionine Threonine Valine Low Isoleucine	unflavoured	12.5g	5g
	**GA explore5** Glutaric Aciduria Type 1 (GA-I)	Lysine Low Tryptophan	unflavoured	12.5g	5g

It is essential that the correct **explore** product is prescribed for the particular condition. To make this easier the **explore** range has been given specific colours according to condition.

* Suitable from 1 year of age.

Notes

Notes

Notes

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