Innovation in Nutrition

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basecal™

The use of **basecal**™ within **nutritional support** in **inborn errors of protein metabolism.**

Vitaflo in Association With You

Supporting education in the dietary management of rare diseases

Disclaimer

These guidelines are for the use of basecal™ in patients with inborn errors of protein metabolism.

These guidelines are based on best practice using published guidelines and recommendations where possible. They should be **read in conjunction with local guidelines** for the dietary management of inborn errors of protein metabolism.

They are **for use by health care professionals** working with this patient group.

These guidelines are **not for use by patients or parents/carers of children** with inborn errors of protein metabolism

They are for general information only and must not be used as a substitute for professional medical advice.

The product information contained in these guidelines, although accurate at the time of publication, is subject to change.

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

Basecal is a food for special medical purposes (FSMP) to be used under medical supervision.

Basecal is not suitable as a sole source of nutrition.

Basecal is suitable for use from 3 years of age.

Collaborators

Vitaflo® dietitians in collaboration with Professor Anita MacDonald PhD, BSc, OBE (Consultant Dietitian, Birmingham Children's Hospital, UK).

Natural protein restriction is commonly advocated for children with inborn errors of protein metabolism. Some children will require a low protein tube feed due to: feeding difficulties associated with neurological complications, poor appetite, avoidance of overnight fasting, maintenance of metabolic control or to prevent metabolic decompensation. For young children there has been limited choice of suitable low protein ingredients and as a consequence, the calculation and preparation of suitable low protein tube feeds has been complex and time consuming for dietitians and nutritionists.

Low protein tube feeds are usually composed of a number of individual modular ingredients. A measured quantity of breast milk, standard infant formula or standard enteral feed may provide any necessary protein requirement. However, the amount of protein-containing formula is limited and it is commonly inadequate to provide total energy and nutrient requirements. Thereby, the rest of the energy and nutrient requirements are composed of modular ingredients of energy (glucose polymer/fat emulsion), micronutrients and electrolytes or they are derived from supplemented protein-free infant formula. Daly[1] reported that a median of four ingredients were added to low protein enteral feeds for children with organic acidaemias. Evans[2] showed that a higher number of feed ingredients was associated with increased feed preparation error. Evans[3] also demonstrated that mothers with limited English language skills were unable to read or understand written feed recipe instructions.

Basecal is a protein-free, powdered module that is pre-measured in a sachet. Its nutritional composition is similar to a standard paediatric enteral feed formula, but it is without protein. At standard dilution, it provides 100 kcal for each 100ml of feed and is supplemented with vitamins, minerals, electrolytes, essential fatty acids and long chain fatty acids. The protein-free module can be given with both natural and precursor-free L-amino acid sources or it can be given as a protein-free feed only.

We now have over four years' experience of using basecal for children requiring low protein tube feeds. Its use has simplified low protein feed preparation. It is safe and is associated with significant improvements in nutritional intake and nutritional biochemistry of patients on low protein or protein-free enteral tube feeds[4]. These guidelines explain the practical use of basecal. They will demonstrate how it can be incorporated into low protein tube feeds for patients with inborn errors of protein metabolism.

Anita MacDonald

Contents

1.0 Introduction

1.1 Introduction to the guidelines

Some individuals with inborn errors of protein metabolism have severe neurological impairment which can lead to feeding difficulties such as vomiting, gastro-oesophageal reflux (GOR), poor appetite, slow feeding and food refusal[5]. Enteral feeding, either total or supplemental, is often essential to maintain an adequate nutritional intake to maintain metabolic stability and achieve optimal growth. Individually and collectively, the management of these patients can be time-consuming and challenging.

Due to the specific unique requirements of these individuals, there is no single, ready-to-use feed that meets all nutritional requirements for patients. Enteral tube feeds therefore may consist of several single modular ingredients combined together. These enteral feeds can be complex to calculate and reconstitute.

These guidelines aim to explain and illustrate how basecal can easily be used as the core ingredient for providing protein free nutrition in a low protein enteral feed, or as a 'top up' supplement.

1.2 Details of basecal

What is basecal?

Basecal is a powdered **protein free feed** containing carbohydrate, fat, vitamins, minerals, trace elements and the long chain polyunsaturated fatty acids (LCPs): arachidonic acid (AA) and docosahexaenoic acid (DHA).

Basecal can be administered via an enteral tube or given orally.

Indications for basecal

Basecal is for use in the dietary management of inborn errors of protein metabolism requiring a low protein diet, and is suitable for use from 3 years of age.

Its main role is as the core ingredient for providing non-protein nutrition in enteral tube feeds in long-term dietary management of inborn errors of protein metabolism.

Overview of nutritional profile

Basecal is a protein free base that is otherwise nutritionally complete. With respect to carbohydrate, fat and micronutrients, its nutritional composition is similar to standard paediatric enteral feeds.

It has a favourable fat profile high in mono-unsaturates and contains both DHA and AA in a 1:1 ratio.

Presentation of basecal

Convenient pre-measured sachets

Basecal sachets facilitate accurate and convenient feed preparation. They are designed to help ensure precise, consistent, simple and quick modular feed preparation. Basecal is presented in two sizes of pre-measured sachets: basecal100 and basecal200, making it easy to calculate the number of sachets required.

Product	Quantity of powder per sachet (g)	Energy per sachet (kcals)	Made up to final volume (mls)	kcals/ml*
Basecal100	21.5	100	100	1
Basecal200	43	200	200	1

* Basecal is reconstituted with water to make up a 1kcal/ml feed. However, it can be made up more or less concentrated as advised by the health care professional (See section 4.0).

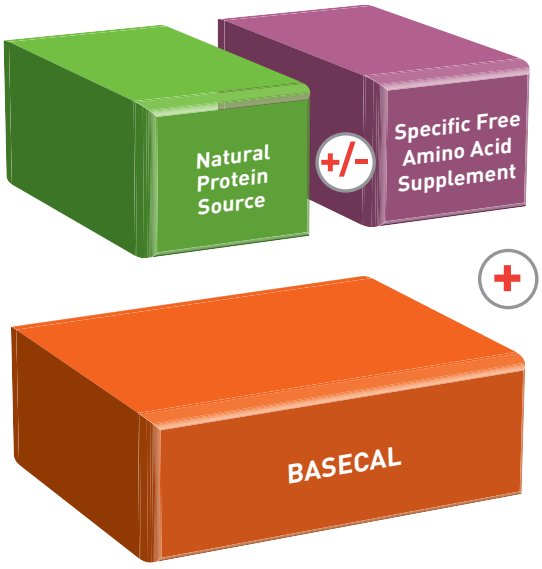
When to use basecal

Basecal can be used in the following ways:

A

As the core ingredient for providing non-protein nutrition in a sole source or supplementary enteral feed, in combination with a protein source to provide protein requirements.

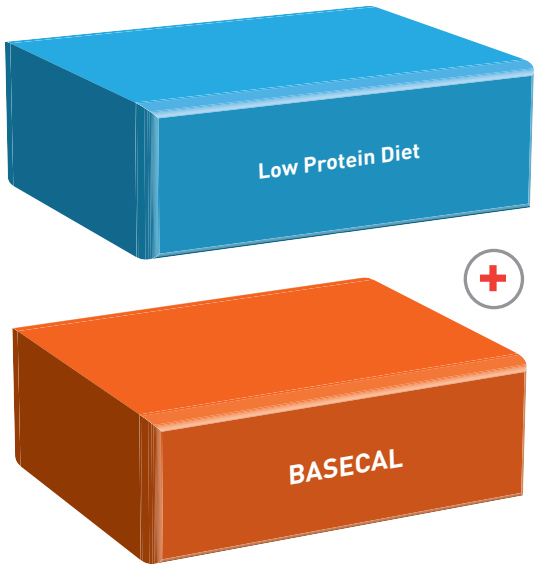
Basecal plus a natural protein source +/- a specific free amino acid supplement (e.g. amino5 range*).



B

As a protein free 'top-up' supplement.

Basecal is given on its own to 'top up' a low protein diet.



* See Appendix 1.

General principles of low protein diets

The general dietary management principles of low protein diets are to:

- **Limit intakes of total natural protein to reduce the production of toxic metabolites.**
- **Provide adequate total daily protein, nitrogen and indispensable amino acids as tolerated by each condition** (see page 17)**.**
- **Provide a disorder specific supplement (either free of the amino acids that cannot be metabolised or as an essential amino acid supplement) as part of total protein requirements as necessary for each condition.**
- **Provide an adequate energy intake:**

  To promote normal growth and development.

  To avoid endogenous protein catabolism which results in an increased production of toxic metabolites e.g. ammonia in urea cycle disorders (UCD).

- **Provide vitamins, minerals and trace elements where indicated.**

  Supplementation is essential as intake is severely limited, particularly in low protein diets based on low biological value protein foods.

- **Assess adequacy and intake of essential fatty acids (EFA) and their longer chain derivatives docosahexaenoic acid (DHA) and arachidonic acid (AA).**

  Deficiency in particular of DHA, has been reported in patients with a UCD or methylmalonic acidaemia (MMA)[6].

When an individual has a good appetite and is able to consume their food orally, they can often meet their energy requirements through dietary advice and appropriate modifications, with the additions of a protein substitute and specialist low protein foods if required.

However, this can be difficult due to the many foods being restricted or other factors such as feeding difficulties. It is when these children and adults are unable to meet their energy and nutritional requirements orally that issues can arise.

There are many factors that can affect nutritional requirements and oral intake. Neurological impairment is common in this patient group and **severe feeding difficulties** have been reported in children with inherited metabolic disorders (IMD) on protein restricted diets[7]. Poor appetites, a poor swallow, gastro-oesophageal reflux, limited food variety and lengthy mealtimes may occur.

Optimal nutritional intake can therefore be difficult to achieve in inborn errors of protein metabolism.

Oral food consumption may be insufficient to adequately meet nutritional requirements.

↓

It is essential that calorie requirements are met at all times.

↓

A lack of calories compromises growth and can cause catabolism.

↓

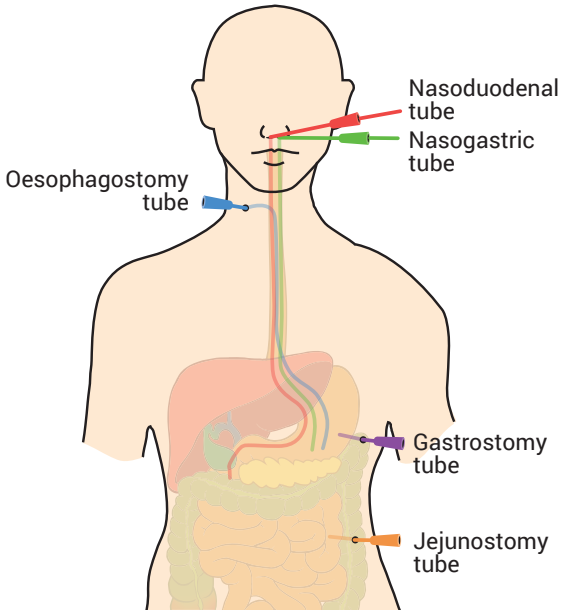
Catabolism leads to increased production of toxins

↓

Ultimately resulting in metabolic decompensation.

Enteral feeding, e.g. via gastrostomy or nasogastric tube, is often essential to provide an adequate dietary intake and prevent metabolic decompensation. It can also provide parents/carers with some respite for children who are difficult to feed[5].

Figure 1. Overview of possible enteral tube feeding routes



It is essential to determine whether enteral tube feeding, either complete or partial, is necessary to prevent catabolism, maintain metabolic stability and promote an optimal nutritional intake and growth.

Nutritional support is crucial for these patients to prevent catabolism and metabolic decompensation.

Examples of disorder types in which nutritional support is often indicated include UCDs and OAs;

- **Urea Cycle Disorders (UCDs):**

  Guidelines published in 2012 for UCDs[8] highlight that enteral tube feeding is important in the following circumstances:

  - **Inability to suck or swallow due to neurological damage or developmental delay**
  - **Severe vomiting, reflux or retching**
  - **Poor appetite and/or refusal of food, essential amino acid (EAA) supplement or medications**
  - **Emergency management during intercurrent illnesses.**

- **Organic Acidaemias (OAs):**

  Guidelines published for methylmalonic acidaemia/propionic acidaemia (MMA/PA) in 2014[9] state that tube feeding is often needed in these conditions, particularly those with severe phenotypes.

  It is emphasised that tube feeding may be necessary to:

  - **Avoid catabolism/prolonged fasting**
  - **Achieve nutritional adequacy**
  - **Administer medications and supplements**
  - **Maintain metabolic stability.**

  The percentage of children and adolescents with MMA or PA requiring tube feeding has been reported to be as high as 50 – 60%[10-12]. A possible higher incidence of feeding problems, and nutritional support with enteral tube feeding occurs in patients with PA.

  The provision of appropriate tube feeds for these patients is challenging. Of all the nutrients, protein provision can be the most variable, as there is no one standard amount that is suitable for all. Individual protein needs not only differ in quantity, but also in the amount of natural protein that is tolerated and additional condition specific free amino acids that may be required.

Due to their complex needs, there is no single, ready-to-use feed that meets all requirements for patients with inborn errors of protein metabolism.

Basecal is designed to provide the core ingredients and additional protein can be added to meet the individual requirements.

2.0 Why use basecal?

General principles of low protein diets	Component of enteral feed
1. **Limit intake of total natural protein** 2. **Provide adequate protein, nitrogen and indispensable amino acids** 3. **Provide a specific free amino acid supplement if required**	**PROTEIN REQUIREMENTS** Natural protein source (+/-) specific free amino acids (e.g. amino5) Needs to be tailored to the individual's needs
4. **Provide an adequate energy intake** 5. **Provide vitamins, minerals and trace elements** 6. **Assess adequacy and intake of EFAs, DHA & AA**	**BASECAL – PROTEIN FREE** **Base of the remainder of feed** The number of sachets can be easily adjusted to meet individual 'non-protein' energy requirements

Feeds made by calculating and combining several separate ingredients is challenging; requiring complicated recipes which are time consuming and potentially inaccurate to prepare.

These separate ingredients are often a mixture of powders and liquids.

Several ingredients may be powders and measured out by scoops of different sizes or by a gram weight scale. Errors in ingredient measuring are common; Gokmen Ozel et al[13] demonstrated that when three different methods of measured powdered ingredients were compared (scoops, scales and sachets), the greatest error resulted from the use of scoops, thus indicating that pre-measured sachets could limit inaccuracy.

A number of additional ingredients for the enteral feed may be liquids, measured in jugs, with the use of a syringe or in measuring cylinders. A study by Evans et al 2011[3] reported as many as 45% of carers inaccurately measured liquid ingredients.

It can be difficult to produce a homogenous feed when combining powder and liquid ingredients.

One study observed, when a 6 separate ingredient feed was prepared, fat adhered to equipment and fat separation occurred in the final prepared feed. Fat levels were therefore significantly lower than expected compared to a 2 ingredient feed, rendering the nutritional content of the feed inaccurate[2]. These losses could potentially be even higher if feeds are administered via an enteral feeding tube which at worst case, may have a detrimental effect on an individual's metabolic stability.

The advantages of using fewer ingredients and also an age appropriate protein free module were further demonstrated in a recent abstract[4]. Daly et al showed that nutritional intake and nutritional biochemical markers significantly improved over an 18 month period using a protein free module (basecal) compared to a multi ingredient modular feed or an infant protein free module.

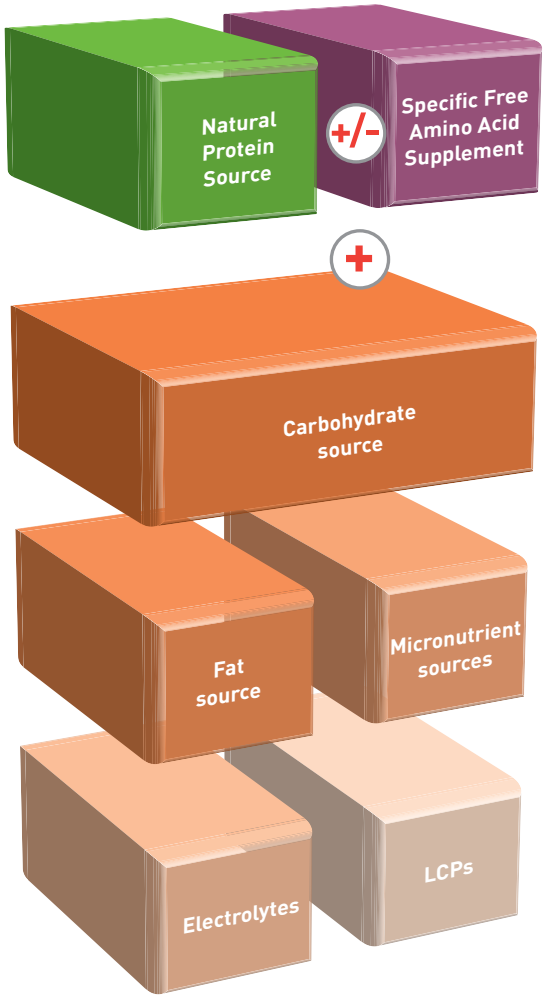
Although it is not possible to have one single ready to use feed that meets all requirements for every individual with inborn errors of protein metabolism, basecal can be used as the core ingredient providing all nutrients (apart from protein) in a pre-measured sachet. This simplifies feed calculations for the health care professional (HCP) and preparation for the patient/carers.

Due to the complex nature of the dietary management of disorders of protein metabolism a bespoke, modular, low protein feed comprising of numerous separate ingredients is commonly required to meet the specific needs of the individual.

Issues with a modular approach

- **Complex feeds –** comprising of up to 7 single ingredients
- **Inaccuracy –** many ingredients require measuring and weighing out. This practice has been proven to increase the risk of error[12]
- **Poor feed homogenisation –** leading to possible nutrient losses left behind on mixing equipment[2]
- **Complex calculations –** as many different products to consider
- **Time consuming –** for both the health care professional and patient/carer
- **Difficult for anyone but key carer to prepare**
- **Difficult to transport numerous ingredients**
- **Increased hygiene risk**

Feed* using separate ingredients

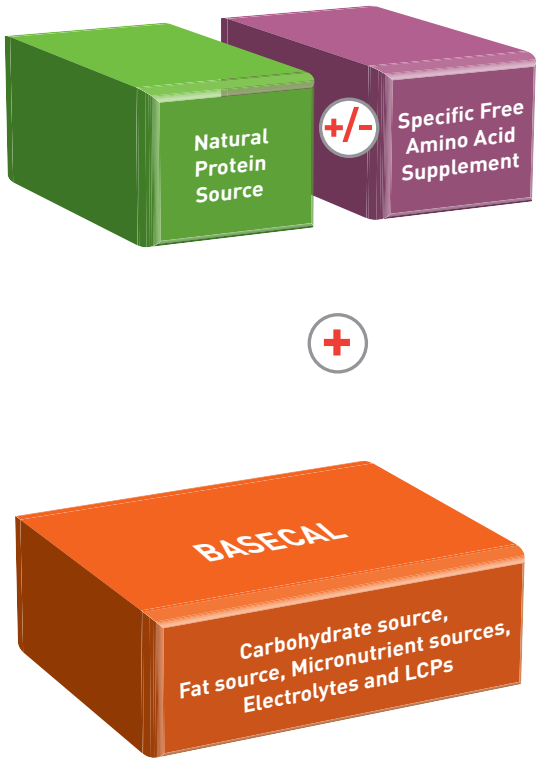


* complete feed when reconstituted with water.

2.3 Basecal simplifies feed preparation.

Basecal reduces the number of separate components needed to make up a feed by combining the carbohydrate, fat, micronutrients, electrolytes and LCPs in a convenient pre-measured sachet.

Feed* using basecal



Advantages of using basecal

- **Simpler feed –** basecal is nutritionally complete (apart from protein) – reducing the number of ingredients required to 2 or 3
- **Convenient pre-measured sachet –** reducing the amount of products that need measuring out
- **Accurate –** exact amount every time; no weighing or scoops required
- **Soluble and mixes well –** to produce a homogeneous feed
- **Simple calculation to adapt the feed –** as the profile is similar to a 1 kcal/ml enteral feed
- **Choice of pack sizes –** feed can be tailor-made to individual requirements
- **Improves nutritional intake and biochemical status**[13]
- **Less wastage -** sachets only opened as required
- **Easier for others to prepare**
- **Easily transportable**
- **Hygienic -** individual, pre-measured sachets

3.0 How to use basecal

3.1 How to calculate an enteral feed

Protein requirements

For OAs and UCDs, a low protein enteral feed or diet should initially ALWAYS aim to meet the minimum safe intake of protein as guided by the FAO/WHO/UNU [2007][14] and then be titrated according to natural protein tolerance[11]. International/national guidelines should be followed for individual conditions when indicated.

These recommended safe intakes of protein have been calculated to meet the protein requirements of most individuals and can be used as an initial guide to determine protein requirements in a low protein diet or feed.

Protein tolerance will depend on the age, gender, physical activity, growth rate, residual enzyme activity and the metabolic stability of the patient. As these factors are not constant, regular clinical and biochemical monitoring, as per local practice, is essential to determine individual protein requirements. Prescribed intakes will need modification over time to take changes into account and will require careful monitoring.

- **PROTEIN is prescribed on an individual patient basis usually as a natural protein source (standard paediatric or adult feed) +/- an additional specific free amino acid supplement.**
- For the purpose of calculations within these guidelines, the enteral feed natural protein values used have been taken from a standard paediatric 1 kcal/ml enteral feed available in the UK.

Energy requirements

The aim is to provide adequate energy to maintain growth, weight gain and metabolic stability. However, children with inborn errors of protein metabolism may have lower requirements (e.g. those with reduced mobility due to physical disability) or higher requirements (e.g. those with severe dystonia). Energy requirements should be determined by age, gender, growth data, diet history, activity and metabolic stability. Excess weight gain should be avoided.

- **Basecal is prescribed to provide the 'non-protein' ENERGY requirements.**
- **Basecal is available in 200 and 100 kcal sachets, making it easy to calculate the number of sachets required.**

Basecal, when combined with the protein source(s), should meet the total daily calculated nutritional requirements* for an enteral feed providing the sole source of nutrition.

It is important that nutritional intakes and growth of patients are assessed regularly to ensure individual needs are met based on age, growth, development, physical activity and metabolic stability.

* Total daily calculated requirements includes those for micronutrients.
Basecal has a comprehensive mineral, trace element and vitamin profile, which, when combined with the protein source(s) to meet energy requirements, will cover micronutrient requirements.

Fluid requirements

Some patients with inborn errors of protein metabolism may require extra fluid. It is particularly important to avoid dehydration in MMA and maintain adequate energy intake[5]. Fluid requirements should be determined on an individual basis.

If normal fluid requirements are indicated, the following guidelines can be used for children (an adaptation of the Holliday-Segar formula)[15].

For children over 10kg

11 - 20kg: 100ml/kg for the first 10kg
+ 50ml/kg for the next 10kg

20kg and above

100ml/kg for the first 10kg
+ 50ml/kg for the next 10kg
+ 25ml/kg thereafter

Example:

An 8 year old boy, weight = 23kg

100ml/kg for the first 10kg = 1000ml
+ 50ml/kg for the next 10kg = 500ml
+ 25ml/kg for the final 3kg = 75ml

Total = 1575ml/day (68ml/kg)

For adults

Normal fluid requirements: 30 - 35ml/kg[16]

Considerations

Overweight child - will require fluid as calculated from above but may require a reduced energy intake.

Underweight child - calculate fluid requirements for the child's actual weight, but may require increased energy for catch up growth.

Monitoring

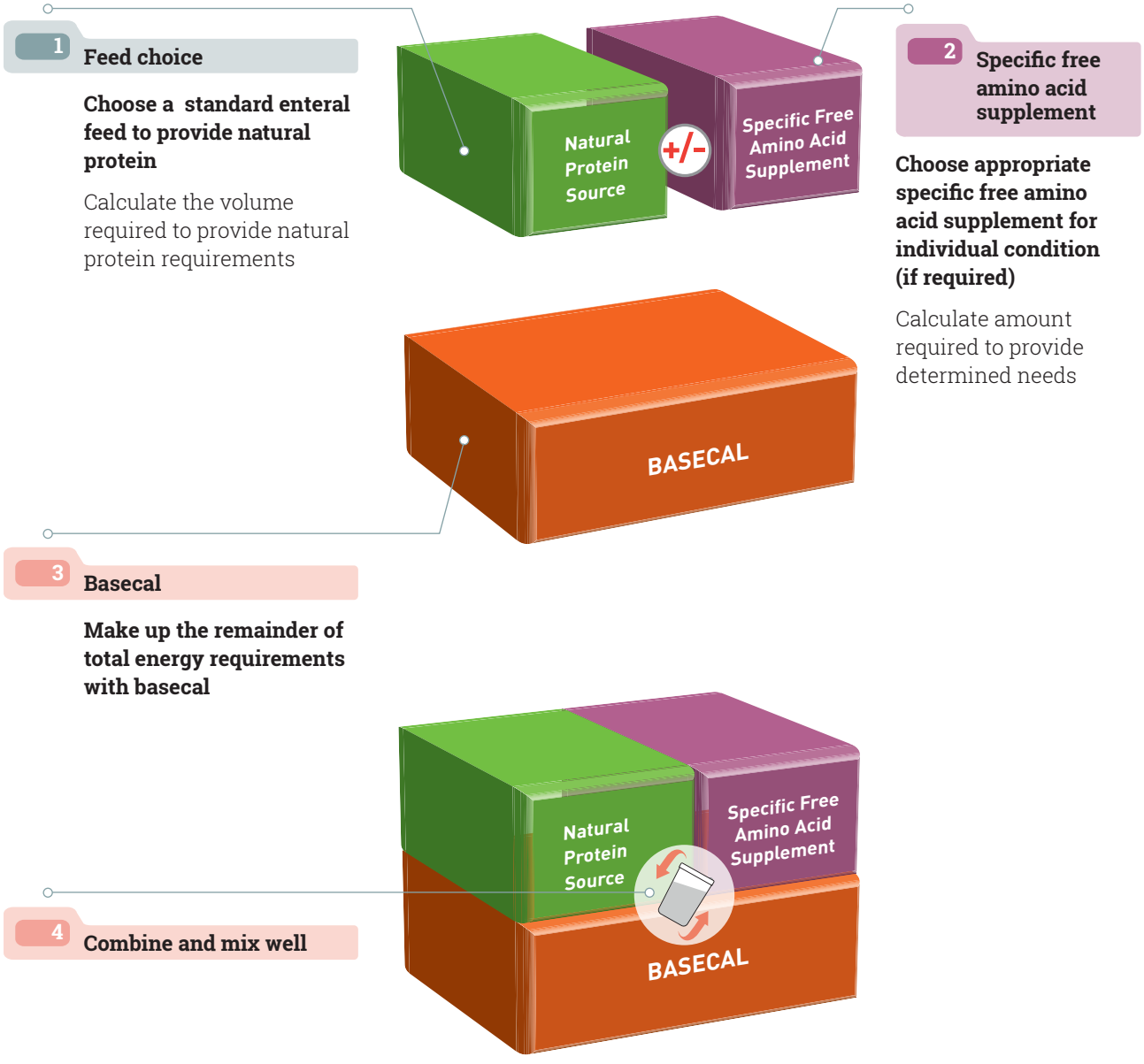
- ☑ **Regularly monitor clinical and biochemical indices to assess adequacy of nutritional intake[17].**
  - Clinical examination of skin and hair specifically looking for signs of protein deficiency (e.g. skin rashes)
  - Anthropometric measurements
  - Weight & length/height plotted on growth chart
  - Dietary intake assessment
- ☑ **If possible carry out annual assessment of[17].**
  - Plasma status of key minerals, trace elements and vitamins
  - Biochemical assessment of quantitative amino acids, markers of protein status, e.g. pre-albumin, and electrolytes
- ☑ **If possible carry out bone mineral density scans at baseline age 11 years and repeat every 5 years in the absence of osteopenia or osteoporosis[17].**

A As the core ingredient for providing non-protein nutrition in a SOLE SOURCE or SUPPLEMENTARY enteral feed

Basecal plus a natural protein source +/- a specific free amino acid supplement (e.g. amino5 range*).

Nutritional assessment

- **Calculate nutritional requirements: energy, protein, fluid, micronutrients (See pages 17-18 for details)**
- **Assess oral nutritional intake**
- **Determine whether a sole source of nutrition or supplementary feed is required**
- **Determine natural protein tolerance and whether a specific free amino acid supplement is needed**



Note:

Check adequate fluid is provided for daily requirement.

- Additional fluid can be given as water flushes or by diluting basecal.
- If fluid is restricted or an individual has high calorie requirements, basecal can be concentrated. See page 39 for more information.

* See Appendix 1.

B **As a protein free 'top-up' supplement.**

Basecal is given on its own to 'top up' a low protein diet.

Nutritional assessment

- **Calculate nutritional requirements: energy, protein, fluid, micronutrients (See pages 17-18 for details)**
- **Assess oral nutritional intake**

Oral low protein diet

When oral intake meets protein needs

1 Feed choice

No natural protein source required as meeting protein requirements orally

2 Specific free amino acid supplement

Not required as meeting protein requirements orally

3 Basecal

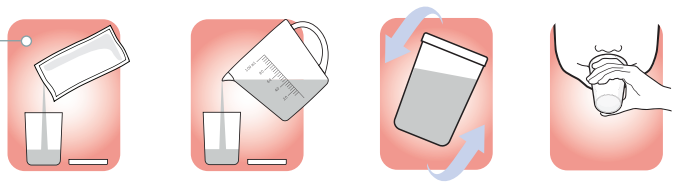
Basecal can be given as an energy and micronutrient 'top up' supplement.

This can be taken orally or via an enteral feeding tube.

As an energy and micronutrient 'top-up' supplement

4 Make up basecal

As per instructions to standard dilution of 1 kcal/ml.



Over the next few pages, worked examples of basecal being used in the different clinical scenarios will be outlined.

3.3 Calculated example 1 - As the core ingredient for providing non-protein nutrition in a SOLE SOURCE enteral feed

A

- **8 year old boy with propionic acidaemia (PA)**
- **Weight = 24kg (Just >25th percentile) Height = 124cm (25th percentile)**

Sam is 8 years old. He was diagnosed with PA at the age of 2 weeks old presenting with severe metabolic acidosis and hyperammonaemia. Sam experienced several episodes of metabolic decompensation within the first year of life and has long standing feeding problems, which resulted in a percutaneous endoscopic gastrostomy (PEG) being inserted at the age of 4 years.

Sam lives with his grandma who is currently making up an enteral feed consisting of 6 separate ingredients and finding it increasingly difficult to prepare each day.

Grandma and Sam attend a clinic to see the dietitian who carried out a nutritional assessment:

Nutritional assessment

	Energy (kcal)	Protein* (g)	Fluid (ml)	Comments
Total provided by current modular feed	1700	24	1700 plus flushes	
Assessment of typical oral daily dietary intake	0	0	0	**Sole source of nutrition required**
Total to be provided by basecal enteral feed	**1700**	**24**	**1700**	
Natural protein tolerance = 20g/day				
Specific free amino acid required: YES - MMA/PA amino5				

* Aiming for 1g protein/kg.

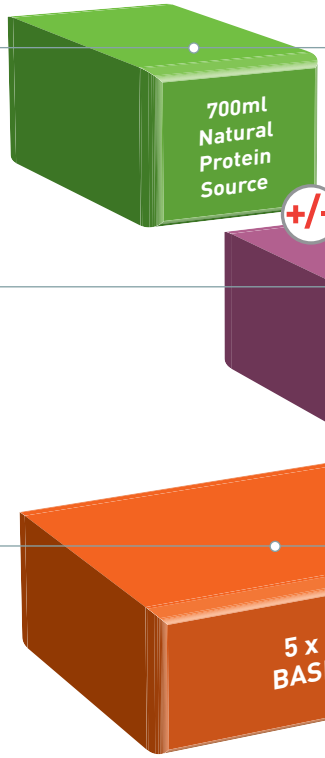
Action:

The dietitian explained that basecal could replace some individual ingredients in the feed. Using basecal meant that only 3 separate ingredients were needed for Sam's feed instead of 6.

- Daily feeds should ideally be evenly distributed over a 24 hour period to meet full calculated requirements. Feeds can be administered either continuously using a feeding pump/ as regular boluses or as a combination of both delivery methods*. This would depend on equipment available or the condition /metabolic stability of the patient.
- It is advantageous to distribute protein requirements over 24 hours.
- If feeding continuously via a pump, follow local and national guidelines for maximum hanging times. It is suggested that a maximum hanging time of 4 hours is applied for reconstituted feeds[18].
- Take into consideration practical aspects of meeting extra fluid requirements. These may be met by diluting the feed or ensuring extra fluid is provided by additional flushes of water through the day.
- Whilst it is essential the patient receives adequate nutrition, the enteral feeding regime should be planned to fit in as much as possible with the family's/patient's lifestyle.

* **Note** if feeding via a jejunostomy/nasoduodenal enteral tube, bolus feeding is not advised[19,20] and sterile water should be used to reconstitute the feed[18].
Always check and follow local and national guidelines for post pyloric feeding.

SOLE SOURCE feed calculation



1 Feed choice

Natural protein tolerance
= 20g/day

700ml standard paediatric 1kcal/ml feed

Energy (kcal)	Protein (g)	Fluid (ml)
700	**19.6**	**700**

2 Specific free amino acid supplement

MMA/PA amino5
= 4.4g PE required

1 x sachet = 5g PE

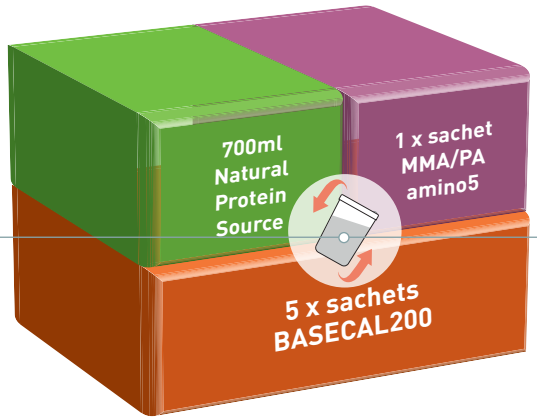
Energy (kcal)	Protein (g)	Fluid (ml)
20	**5**	**0**

3 Basecal

Remainder kcal required from basecal
= 980kcal required

5 x sachets basecal200

Energy (kcal)	Protein (g)	Fluid (ml)
1000	**0**	**1000**



4 Combine and mix well

Total Feed=

Energy (kcal)	Protein (g)	Fluid (ml)
1720	**24.6**	**1700**

Dietetic Follow Up:

Sam and his grandma returned to clinic 1 month later for review. Sam's grandma had completed the transition of Sam's feed over to using basecal and found the fewer ingredients much easier to prepare. Sam was tolerating the feed well and following appropriate growth percentiles.

3.3 Calculated example 2 - As the core ingredient for providing non-protein nutrition in a SUPPLEMENTARY enteral feed

A

- **4 year old girl with isovaleric acidaemia (IVA)**
- **Weight = 13.5kg (just >9th percentile) Height = 99cm (Just < 25th percentile)**

Lily is 4 years old. She was diagnosed with IVA within the first week of life presenting with vomiting, refusal of feeds and metabolic acidosis. Lily has been on a modest protein restriction of around 2g/kg/day. Her oro-motor skills and appetite had always been poor and she had been tube fed approximately 50-60% of her nutritional requirements since infancy with the remainder taken orally.

Lily attended clinic with her mum to see the dietitian who carried out a nutritional assessment.

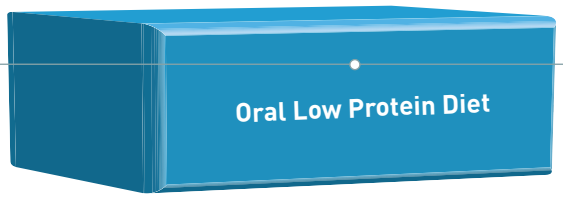
Nutritional assessment

	Energy[21] (kcal)	Protein (g)	Fluid[15] (ml)	Calcium[22] (mg)	Iron[22] (mg)	Comments
Total calculated requirements/day	1290	27	1175	450	6.1	
Assessment of typical oral daily dietary intake	500	17	300	80	1	**Supplementary feed required**
Total to be provided by enteral feed	**790**	**10**	**875**	**370**	**5.1**	
Natural protein tolerance = 27g/day						
Specific free amino acid supplement required: NO						

Action:

Lily has eaten very little orally over the past few months and her weight has dropped slightly. The dietitian advised to increase the energy intake in the feed. The enteral feed will now provide approximately 70% of her nutritional requirements whereas previously it only provided 50-60%.

Oral low protein diet



Energy (kcal)	Protein (g)	Fluid (ml)
500	**17**	**300**

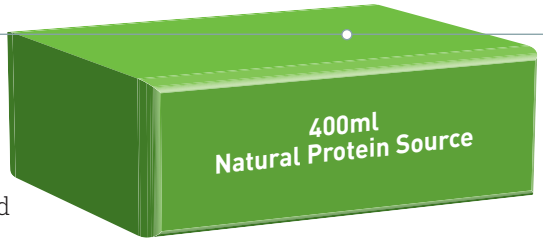
Calcium (mg)	Iron (mg)
80	**1**

+

SUPPLEMENTARY feed calculation

1 Feed choice

Natural protein tolerance
= 27g/day. Taking 17g orally
= 10g protein needed from feed



400ml standard paediatric 1kcal/ml feed

Energy (kcal)	Protein (g)	Fluid (ml)
400	**11.2**	**400**

2 Specific free amino acid supplement

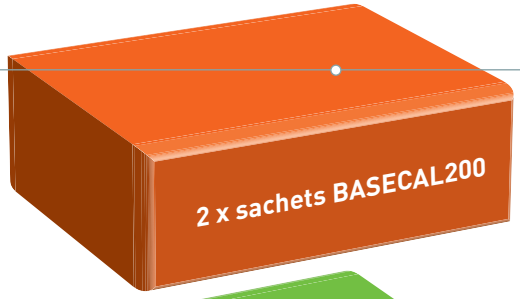
No leucine-free amino acids prescribed.

Not required

+

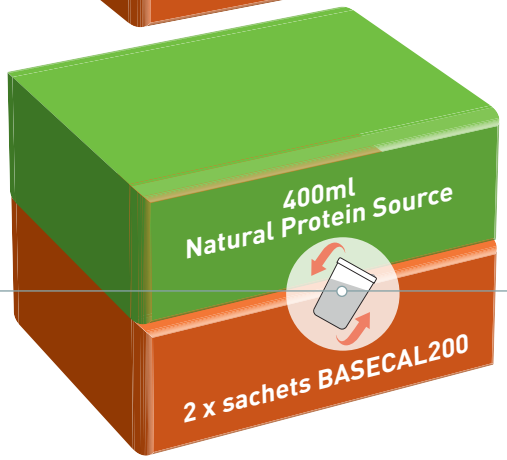
3 Basecal

Remainder kcal required from basecal
= 390kcal



2 x sachets basecal200

Energy (kcal)	Protein (g)	Fluid (ml)
400	**0**	**400**



4 Combine and mix well

Total Feed=

Energy (kcal)	Protein (g)	Fluid (ml)
800	**11.2**	**800**

Calcium (mg)	Iron (mg)
472	**8**

Provide extra fluid with flushes.

Dietetic Follow Up:

The dietitian advised to continue to encourage food orally in the day and to monitor intake. A review appointment was made for a month's time to assess growth, oral intake and feed volumes.

3.3 Calculated example 3 - Incorporating basecal100 into the feed

Basecal100 enables the health care professional (HCP) to tailor an enteral feed to the specific needs of the metabolic patient.

As growth is monitored, it is important to reassess and calculate nutritional requirements. Energy requirements of the patient with inborn errors of protein metabolism can be challenging to estimate. Adjustments in energy intake may therefore need to be gradual to avoid rapid weight gain or loss.

Basecal100 gives the flexibility of adjusting the energy intake in a stepwise manner, whilst providing the majority of non-protein calories with basecal200.

Example:

- **3.5 year old boy with ornithine transcarbamoylase (OTC) deficiency**
- **Weight = 16kg (50 – 75th percentile) Height = 99.5cm (Just <50th percentile)**

Mohammed is 3.5 years old. He was diagnosed with OTC deficiency within the first week of life presenting with acute neonatal encephalopathy and hyperammonaemia. He has severe developmental delay with a poor swallow and had a gastrostomy placed at the age of 15 months. He has been tolerating his feeds well, however over the last 2 months his weight has increased. The dietitian adjusted his feed last month and is reviewing Mohammed's feeding regimen on a monthly basis.

Mum and Mohammed attended the clinic to see the dietitian for their monthly review:

Nutritional assessment

	Energy[21] (kcal)	Protein[14] (g)	Fluid[15] (ml)	Comments
Total calculated requirements/day	1300	14.4	1300	
Assessment of typical oral daily dietary intake	0	0	0	**Sole source of nutrition required**
Total provided by current enteral feed	**1170**	**14.8**	**1150 & 150ml as water flushes**	
Natural protein tolerance = 10g/day				
Specific free amino acid supplement required: YES - UCD amino5				

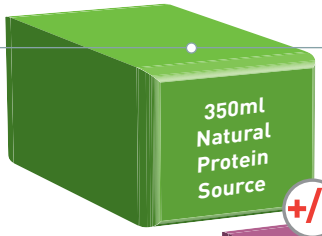
Action:

The dietitian explained that Mohammed's weight had increased by 0.3kg over the last month and advised a further gradual reduction in his total energy intake by 100kcal.

A Current feed:

1 Feed choice

Natural protein tolerance
= 10g/day

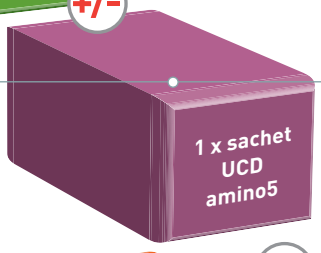


350ml standard paediatric 1kcal/ml feed

Energy (kcal)	Protein (g)	Fluid (ml)
350	**9.8**	**350**

2 Specific free amino acid supplement

UCD amino5
= 5g PE required



1 x sachet = 5g PE

Energy (kcal)	Protein (g)	Fluid (ml)
20	**5**	**0**

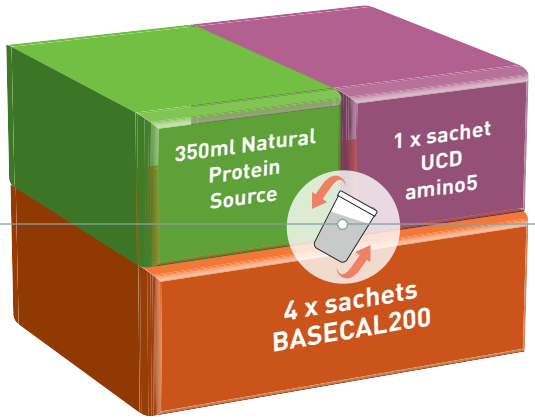
3 Basecal

Remainder kcal required from basecal
= 800kcal

4 x sachets basecal200

Energy (kcal)	Protein (g)	Fluid (ml)
800	**0**	**800**

4 Combine and mix well

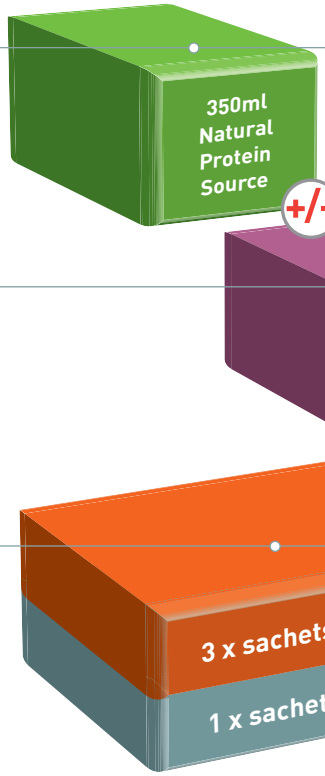


Total Feed=

Energy (kcal)	Protein (g)	Fluid (ml)
1170	**14.8**	**1150**

150ml of fluid is provided as a water flush

B **New feed calculation to provide 100kcal less than the current feed:**



1 Feed choice

Natural protein tolerance
= 10g/day

350ml standard paediatric 1kcal/ml feed

Energy (kcal)	Protein (g)	Fluid (ml)
350	**9.8**	**350**

2 Specific free amino acid supplement

UCD amino5
= 5g PE required

1 x sachet = 5g PE

Energy (kcal)	Protein (g)	Fluid (ml)
20	**5**	**0**

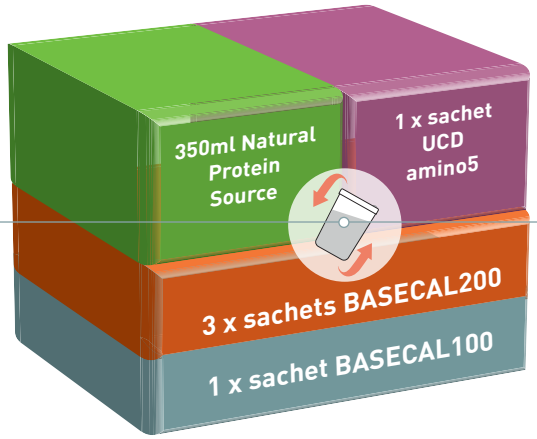
3 Basecal

Remainder kcal required from basecal
= 700kcal

3 x sachets basecal200 **= 600kcal**

1 x sachet basecal100 **= 100kcal**

Energy (kcal)	Protein (g)	Fluid (ml)
700	**0**	**700**



4 Combine and mix well

Total Feed=

Energy (kcal)	Protein (g)	Fluid (ml)
1070	**14.8**	**1070**

Provide extra fluid with 250ml as water flushes

Dietetic Follow Up:

Mohammed and his mum returned to clinic 1 month later where Mohammed's weight was beginning to stabilise and he was tolerating his feed well.

3.3 Calculated example 4 - As a protein free 'top-up' supplement

B

- **9 year old boy with glutaric aciduria type 1 (GA1)**
- **Weight = 24.2kg (just >9th percentile) Height = 134cm (50th percentile)**

Ben is 9 years old. He was diagnosed with GA1 at birth following a sibling diagnosis. Ben was started on a low protein diet at the time of diagnosis and had good adherence during early childhood allowing good development and progress at school, neurologically Ben is okay with no issues. He took lysine-free, low tryptophan amino acids until the age of 6 years, but these were stopped after this time.

Ben follows a low protein diet, but he has always had a small appetite and there had been concern about the nutritional adequacy of his diet.

At hospital appointments he has consistently followed the 25th percentile for weight and 50th percentile for height. Over the last 6 months his height has remained stable on the 50th percentile but his weight has slowly decreased to the 9th percentile. He was able to meet his protein requirements via oral diet but it was mostly through processed foods and limited amounts of dairy products. His parents and dietitian were worried about his energy and micronutrient intake but he was unable to tolerate vitamin and mineral supplements. Ben feels he is unable to increase the amount of food he is currently eating.

Ben and his mum saw the dietitian at clinic, who undertook a nutritional assessment.

Nutritional assessment

	Energy[21] (kcal)	Protein[14] (g)	Fluid[15] (ml)	Calcium[22] (mg)	Iron[22] (mg)	Comments
Total calculated requirements/day	1525 + 20% catch up **= 1830**	22	1600	550	8.7	
Assessment of typical oral daily dietary intake	1400	25	1100	300	4	**'Top-up' supplement required**
Shortfall of nutrients	**430**	**0**	**500**	**250**	**4.7**	

Oral Low protein diet

Energy (kcal)	Protein (g)	Fluid (ml)
1400	**25**	**1100**
Calcium (mg)	Iron (mg)	
300	**4**	

1 Feed choice

No natural protein source required as meeting protein requirements orally

2 Specific free amino acid supplement

Not required

3 Basecal

Shortfall of kcal intake orally **= 430kcal**

2 x sachets basecal200

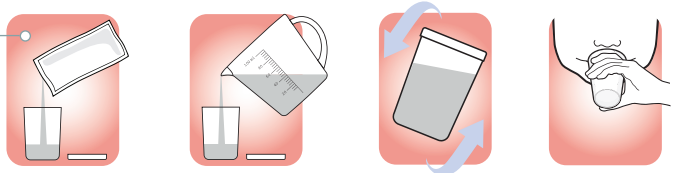
Total 'top up' supplement =

Energy (kcal)	Protein (g)	Fluid (ml)
400	**0**	**400**
Calcium (mg)	Iron (mg)	
232	**4**	

As a 'top-up' supplement feed calculation

4 Make up basecal

As per instructions to standard dilution of 1kcal/ml.



3.3 Calculated example 4 - As a protein free 'top-up' supplement.

Basecal used as a 'top up' supplement on its own

Action:

In order to combine the extra energy and micronutrient requirements Ben was advised by the dietitian to start on basecal200, 2 sachets per day. He was advised to take 1 sachet in the morning before school and 1 sachet after school or in the evening to provide him with an additional 400kcal plus vitamins, minerals and trace elements over the course of the day.

Ben took his morning drink of basecal with no additional flavourings but for the evening drink added either a flavoured strawberry syrup or a protein free milk flavouring.

The table below shows the additional micronutrients provided by the 2 sachets of basecal200. These values have been compared against the age appropriate United Kingdom Dietary Reference Values (DRV)[22] for a 7 - 10 year old, to show what percentage of the RNI is provided by the two sachets.

Nutritional assessment

Nutrient	Unit	Nutrients provided by 2 sachets of basecal200	% of RNI provided by 2 sachets of basecal200
Vitamins			
Thiamin	mg	0.44	63
Riboflavin	mg	0.62	62
Niacin	mg	4.4	37
Vitamin B_6	mg	0.52	52
Folate	µg	74	49
Minerals			
Sodium	mg	168	14
Potassium	mg	400	20
Calcium	mg	232	42
Phosphorus	mg	168	37
Magnesium	mg	40.8	20
Trace elements			
Iron	mg	4.0	46
Copper	µg	0.28	40
Zinc	mg	4.0	57
Iodine	µg	68	62
Selenium	µg	12	40

Dietetic Follow Up:

On his next return to clinic 3 months later, Ben's weight had increased to the 25th percentile whilst his height remained on the 50th per centile.

Ben is currently happy to continue taking 2 sachets of basecal200. He remains under regular dietetic review.

Use within an enteral feed:

When changing a patient from their usual modular feed onto basecal for the first time:

- Introduce basecal systematically over a period of 3 – 4 weeks
- Gradually replace the energy in the usual feed with basecal – e.g. 1 sachet/week and reduce the carbohydrate and fat sources accordingly.
- Ingredients in the usual modular feed such as vitamins, minerals and LCPs can be stopped in week 1. These do not significantly affect energy intake and are present in basecal, therefore any deficit will only be very short term.
- Monitor stool output, abdominal pain, vomiting, weight gain or loss.

Example feed titration

Low protein feed for a 5 year old girl. Weight = 17kg

Ingredient	Usual feed	Week			New Feed with basecal
		1	2	3	4
Natural protein source (ml)	500 (500kcal)	500	500	500	500
Carbohydrate (CHO) powder* (g)	140 (532kcal)	110	70	30	0
Fat emulsion* (ml)	50 (225kcal)	40	30	20	0
Vitamin & mineral powder* (g)	6 (28.8kcal)	✖	0	0	0
Sodium solution (ml)	110	✖	0	0	0
Potassium chloride solution (ml)	9	✖	0	0	0
LCPs* (g)	4 (16kcal)	✖	0	0	0
Basecal200 sachet/s	0	**1**	**2**	**3**	**4**
Total energy (kcal)	**1304**	**1298**	**1301**	**1304**	**1300**
Total protein (g)	**14**	**14**	**14**	**14**	**14**

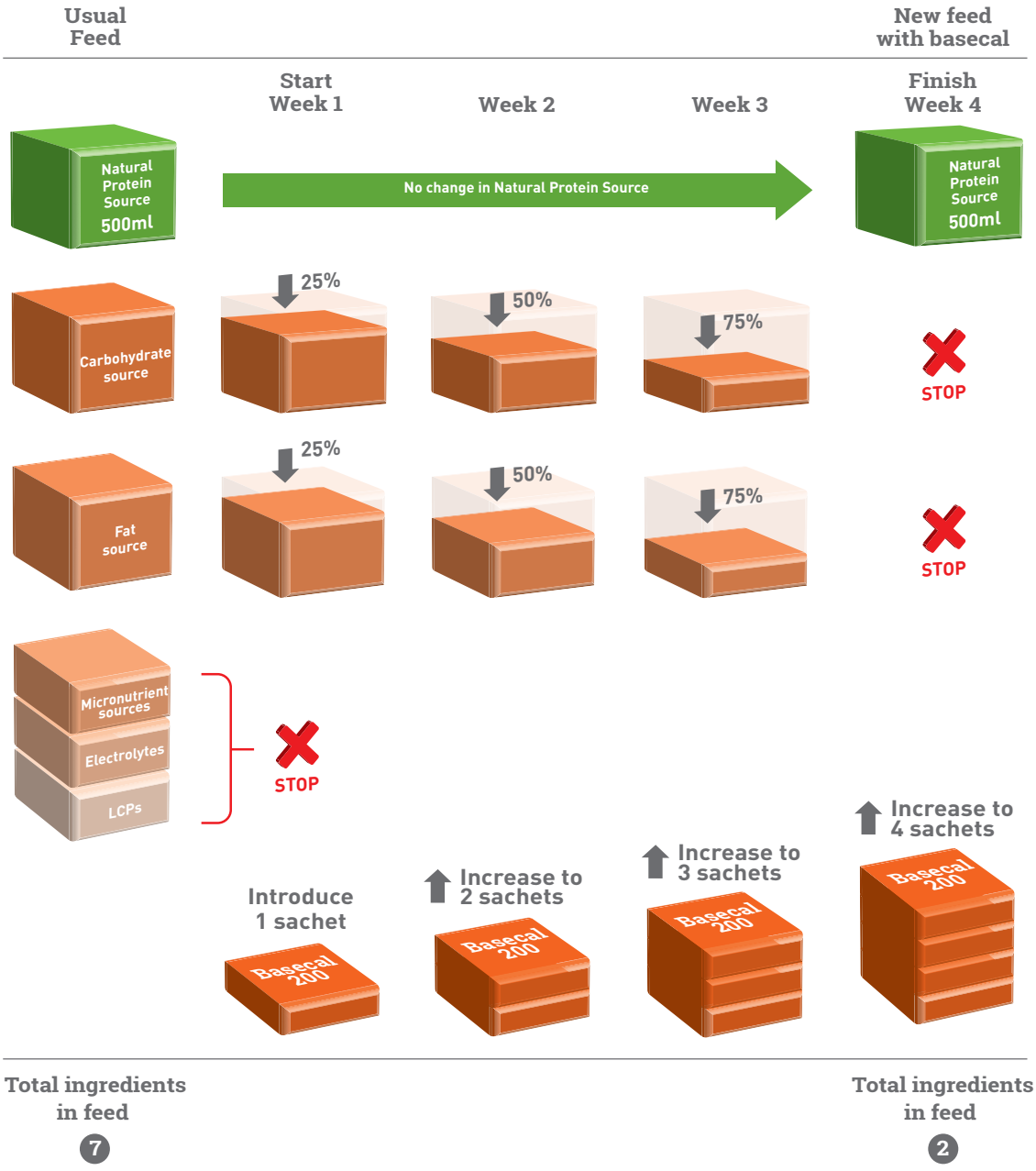
* figures used within the calculation have been taken from products available in the UK.

Note: Ensure the correct amount of water is measured out during the transition to make up the feed – errors commonly occur resulting in a more concentrated/diluted feed which could affect tolerance.

Use as an oral 'top up' supplement

Permitted flavours can be added to reconstituted basecal to aid palatability/variety e.g. protein-free fruit or coffee flavoured syrups or powders.

Transitioning from multiple ingredients to using basecal



General products tips

- **Encourage families to stock rotate at home to ensure no product remains at the back of the storage cupboard and goes out of date.**
- **Encourage home delivery of products if available.**
- **Ensure basecal100 and basecal200 sachets are not mixed and stored in the same box.**

4.0 Preparation guidelines

4.1 Preparation guidelines

- **A** As the core ingredient for providing non-protein nutrition in a SOLE SOURCE or SUPPLEMENTARY enteral feed
- **B** As a protein free 'top-up' supplement

4.2 Concentrating basecal

A **As the core ingredient for providing non-protein nutrition in a SOLE SOURCE or SUPPLEMENTARY enteral feed**

Basecal + **Natural Protein** +/- **Specific Free Amino Acid Supplement (e.g. amino5*)**

Wash hands and ensure equipment is clean.

1. Measure out the prescribed volume of natural protein source required in a large measuring jug.

2. Empty contents of prescribed number of basecal sachets into the same large measuring jug. Add the amount of specific free amino acid supplement prescribed (if required) to the same large measuring jug.

3. Top up with cold water to the final required volume and mix well.

Note: This is one way of making up an enteral feed using basecal, a natural protein source +/- a specific free amino acid supplement. Local, national and international practice may vary.

Note: If feeding continuously via a pump, follow local and national guidelines for maximum hanging times.

* See Appendix 1.

B As a protein free 'top-up' supplement

For 1kcal/ml dilution

basecal 100

basecal 200

Wash hands and ensure equipment is clean.

1. Empty the contents of the sachet into a beaker.

2. Add cold water:

↘ For basecal100 fill to a final volume of 100ml.

↘ For basecal200 fill to a final volume of 200ml.

3. Replace lid and shake well for 10 seconds.

4. Basecal is now ready to use.

For best results, basecal should be freshly prepared and where possible used immediately. Any unused basecal should be refrigerated. Discard any remaining product 24 hours after preparation.

Permitted flavourings can be added to reconstituted basecal to aid palatability or variety e.g. protein-free fruit or coffee flavoured syrups or powders.

4.2 Concentrating basecal

It may sometimes be necessary to concentrate basecal due to fluid restriction, or if an individual has high/very high energy requirements. In these cases the total volume of feed may be excessive when prepared at a 1kcal/ml dilution.

It should be noted that concentrating basecal affects the osmolality and how an individual may tolerate the feed. Concentrating feeds should be done in a stepwise manner, monitoring gastrointestinal tolerance and metabolic stability.

The following table provides osmolality comparisons to those of standard feeds (paediatric and adult) of equivalent kcal/ml concentration:

Basecal Concentration (kcal/ml)	Basecal Osmolality (mOsm/kg)	Paediatric Equivalent (kcal/ml) standard enteral feed Osmolality (mOsm/kg)	Adult Equivalent (kcal/ml) standard enteral feed Osmolality (mOsm/kg)
1.0	315	275	305
1.25	447	426*	440 (1.2kcal/ml)
1.5	598	390	460
2.0	929	NA	470

*figure taken from a whole protein product with 25% of fat as MCT.

If preparing basecal as a 'top up' supplement, the below table gives guidance on how much water to add to a sachet to yield a specific concentration.

Preparation guidance for concentrating basecal

Concentration (kcal/ml)	Basecal100 Water (ml) to add to 1 sachet	Basecal100 Final volume (ml)	Basecal200 Water (ml) to add to 1 sachet	Basecal200 Final Volume (ml)
1.0	85	100	165	200
1.25	65	80	130	160
1.5	55	67	110	134
2.0	40	50	75	100

Paediatrics: for children ≥ 3 years old:

Fat concentrations of above 7% (7g/100ml) may induce a feeling of nausea and cause vomiting[15].

Basecal contains at 1kcal/ml – 15g carbohydrate/100ml, 4.5g fat/100ml

5.0 Guideline references

1. Daly A, Evans S, Gerrard A, Santra S, Vijay S, MacDonald A. The Nutritional Intake of Patients with Organic Acidaemias on Enteral Tube Feeding: Can We Do Better? JIMD Rep. 2015;28:29-39.
2. Evans S, Daly A, Ashmore C, Gokmen-Ozel H, Dileva R, Dumbleton B, et al. Nutritional content of modular feeds: how accurate is feed production? Arch Dis Child. 2013;98(3):184-8.
3. Evans S, Preston F, Daly A, Neville C, MacDonald A. Accuracy of home enteral feed preparation for children with inherited metabolic disorders. J Hum Nutr Diet. 2011;24(1):68-73.
4. Daly A, Evans S, Ashmore C, MacDonald A. O-007 Longitudinal study examining nutritional status in children with organic acidaemias on a modular feed using a protein free module especially developed for children with IMD (Abstract). J Inherit Metab Dis. 2016;39:S37.
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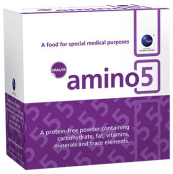
6.0 Appendices

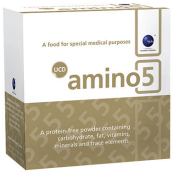
In certain conditions, specific free amino acid supplements may be used to provide a certain percentage of calculated protein requirements. In the case of some organic acidaemia conditions these can be precursor free amino acid supplements (i.e. free of the amino acids which cannot be metabolised) or as an essential amino acid (EAA) supplement; in the case of urea cycle disorders. The amount advised, and in which particular patients these are prescribed to, varies considerably dependent on the individual and local or national practice.

Vitaflo International Ltd has a range of disorder specific amino acid supplements that can be used in conjunction with basecal.

Like basecal, amino5s are in pre-measured sachets. Each sachet contains 5g protein equivalent (PE), aiding accuracy, safety and ease of use with regard to calculation and preparation of feeds. The amino5s are suitable from 3 years onwards.

Amino5s are available for the following disorders:





Product	MMA/PA amino5	MSUD amino5	UCD amino5	GA amino5
Disorder	Methylmalonic Acidaemia / Propionic Acidaemia (MMA/PA)	Maple Syrup Urine Disease (MSUD)	Urea Cycle Disorders (UCD)	Glutaric Aciduria Type 1 (GA)
Sachet Size (g)	6	6	6.6	6
Quantity of Protein Equivalent (g)	5	5	5	5
Free From:	Methionine, Threonine & Valine. Low Isoleucine	Leucine, Isoleucine & Valine	Non Essential Amino Acids	Lysine. Low Tryptophan

Calculate amount of amino5 required FIRST if:

- The amino5 product is to provide a certain percentage of total calculated protein requirements, with the natural protein source topping up to meet total protein requirements.

Calculate amount of natural protein source required FIRST if:

- The natural protein source is to meet a tolerated natural protein amount/calculated essential requirements of a restricted amino acid, with the amino5 product topping up to meet total protein requirements.

Note:

Local and international guidelines should be consulted to aid the decision on whether an amino5 product is required and how much to advise.

Studies showing the inaccuracy of a modular approach, using numerous separate ingredients:

Two studies by Evans et al[1, 2] investigated 40 and 52 patients respectively, with inherited metabolic disorders (IMD) who were tube fed at home. A practical assessment of feed preparation and storage at home was undertaken. The main issues identified were; almost half of the participants measured ingredients inaccurately; half of those who used scoops did not use them correctly, some even used the wrong scoop; hygiene practices were poor and there was incorrect storage of opened unused ingredients.

The same authors then carried out a prospective, observational study in 2013[3] examining the accuracy of modular feed preparation for children with complex medical conditions requiring specialist feeds.

Participants were eligible if they had prepared daily modular feeds at home consisting of ≥ 2 ingredient feeds for ≥ 3 months and they had been previously trained and considered competent in feed preparation by the hospital's special feed unit.

52 participants were studied: one patient and 51 caregivers. The median number of feed ingredients in their usual feed was 4 (range 2 – 7). The components were a mixture of powders and liquids that needed to be measured out at home using scoops, measuring scales, jugs and syringes.

In the study participants were observed making 2 feeds: a 2 ingredient and a 6 ingredient feed. Initially this was done at a research centre with special feed making facilities and then it was repeated, 8 weeks later, at home. The same feeds were prepared by a trained feed maker as a control.

The study showed that feed preparation was particularly inaccurate when 6 ingredients were required. Ingredients were poorly measured, equipment was used inaccurately and there was inadequate ingredient mixing, leaving residue on the equipment. Even amongst trained feed makers, the feeds did not match the calculated nutrient analysis of ingredients. The study suggested that although there was some participant incompetency, there were other factors (including equipment inaccuracy, nutrient losses through preparation technique and poor ingredient emulsification) all causing feed composition error even for experienced feed makers.

The advantages of using fewer ingredients and an age appropriate protein free module were further demonstrated in terms of nutritional intake in a recent abstract[4]. Thirteen children aged 3-15 years replaced either an infant protein free module or several separate modular ingredients with basecal for a period of 18 months. Compared with baseline results, the dietary intakes of numerous micronutrients improved including: calcium, magnesium, iron, zinc and selenium. All nutritional biochemical biomarkers improved, with significant improvements in zinc, vitamin B12 and mean corpuscular volume (MCV).

The conclusions of these studies were:

- **There are several significant safety issues associated with home enteral tube feeding in IMD including: poor hygiene, inaccurate ingredient measuring, poor ingredient emulsification, poor feed preparation methodology, inappropriate storage and long feed hanging times.**
- **The above issues in the preparation of modular home enteral tube feeds increases both metabolic and microbial risk.**
- **There is a need for pre-measured or combined ingredient preparations in sachets, to maximise feed accuracy, improve long term nutritional intake and minimise clinical risk.**

Appendix 2 References

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