

Guideline on prescribing infant formula for infants with Cows' Milk Protein Allergy (CMPA)

Produced by: Dietitians Joanna Padfield, Sue Perry, Ravina Krishan and the Medicines Management team, as a part of collaborative working between NHS Barking and Dagenham, Havering and Redbridge Clinical Commissioning Groups (BHR CCGs) and NHS North East London Foundation Trust (NELFT)

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Aim of the guidelines

To provide GPs and allied health professionals with guidelines on the safe, appropriate and cost effective initiation and monitoring of infant formula for children with cows' milk protein allergy (CMPA).

Objectives

1. To understand the:
 - Type and quantity of formula to prescribe
 - Range of products available and their costs
 - Criteria for referral to the Community Nutrition and Dietetics Service and/or secondary/specialist care
 - Review process and criteria for discontinuing prescriptions
2. To be able to access the evidence base for the guidelines.

Introduction

It is estimated that 1.9 - 4.9 percent of infants and young children have cows' milk protein allergy (CMPA), making it one of the most common food allergies in this age group (Venter C, Arshad SH; 2011). Specialised hypoallergenic formulas can be prescribed for infants with CMPA in order to resolve symptoms and ensure optimal growth and development (Fiocchi A et al; 2010). There are 2 main types of hypoallergenic formulae:

- **Extensively hydrolysed formulas (EHF).** The protein is broken down into peptides. These are tolerated by 90% of infants with CMPA (Allen KJ, Davidson GP, Day AS, et al; 2009).
- **Amino acid formulas (AAF).** The protein is broken down into individual amino acids. They provide an alternative for children who do not tolerate EHF or those with severe symptoms.

Lactose intolerance

Lactose intolerance occurs when the infant has insufficient lactase enzyme to be able to digest milk sugar. The symptoms of lactose intolerance include stomach pain, diarrhoea, a bloated stomach and excessive wind. These symptoms usually occur within 1–3 hours after taking milk. In this case, the infant will require a lactose free formula, **Extensively Hydrolysed Formulae (EHF) or Amino Acid Formulae (AAF)** are not required unless **CMPA** is also present.

****Please note that Lactose Intolerance is not the same as CMPA****

Breast milk first

Breast milk remains the optimal milk for infants. This should be promoted and encouraged where it is clinically safe to do so and the mother is in agreement.

Signs and symptoms

Most infants with CMPA develop symptoms within 1 week of introduction of a CMP - based formula.

Signs and symptoms of possible food allergy (NICE guidelines CG116; 2011)

IgE-mediated	Non-IgE-mediated
The skin	
Pruritus	Pruritis
Erythema	Erythema
Acute Urticaria – localised or generalised	Atopic eczema
Acute angioedema – most commonly of the lips, face and around the eyes	
The Gastrointestinal system	
Angiodema of the lips, tongue and palate	Gastro-oesophageal reflux disease
Oral pruritus	Loose or frequent stools
Nausea	Blood and/or mucus in stools
Colicky abdominal pain	Abdominal pain
Vomiting	Infantile colic
Diarrhoea	Food refusal or aversion
	Constipation
	Perianal redness
	Pallor and tiredness
	Faltering growth in conjunction with at least one or more gastrointestinal symptoms above (with or without significant atopic eczema)
The respiratory system (usually in combination with one or more of the above symptoms and signs)	
Upper respiratory tract symptoms (nasal itching, sneezing, rhinorrhoea, or congestion [with or without conjunctivitis])	
Lower respiratory tract symptoms (cough, chest tightness, wheezing or shortness of breath)	
Other	
Signs or symptoms of anaphylaxis or other systemic reactions	

Refer to NICE guideline CG116 'Food Allergy in Children and Young People' Feb 2011 for full details on symptoms and diagnosis.

Treatment

Breastfeeding

- Although only 0.5% of exclusively breastfed infants show reproducible reactions to cows' milk protein (CMP), symptoms may present as they react to the milk protein from the maternal diet (Vandenplas et al 2007). Breastfeeding should be encouraged to continue, and a maternal CMP exclusion diet trialled for a **minimum of 2 weeks**. Breastfeeding mothers on a CMP exclusion diet should be assessed to ensure the maternal diet is adequate and may require supplementation with 1000mg calcium per day.

Formula feeding

If the mother is NOT breastfeeding, Extensively Hydrolysed Formulae (EHF) should be prescribed as the first line.

Extensively Hydrolysed Formulae (EHF)

EHF	Age group	Cost (September 2015)
First line and alternatives		
First Line: Similac Alimentum[®] (Abbott)	from birth	400g = £9.10
Nutramigen 1 [®] (Mead Johnson)	from birth	400g = 10.87
Nutramigen 2 [®] (Mead Johnson)	from 6 months	400g = 10.87
Lactose containing formulas These may be used where gastrointestinal symptoms are NOT present		
Aptamil Pepti 1 [®] (Milupa)	from birth	400g = £9.74 800g = £19.40
Aptamil Pepti 2 [®] (Milupa)	from 6 months	400g = £9.29 800g = £18.58
SMA Althera [®] (Nestle Health Science)	from birth	450g = £10.68
EHF with medium chain triglycerides. <u>Should only be started in secondary care.</u> May be used where CMPA is accompanied by malabsorption		
Pregestimil Lipil [®] (Mead Johnson)	from birth	400g = £12.06
Pepti Junior [®] (Cow and Gate)	from birth	450g = £12.89

Amino Acid Formulae (AAF)

AAFs are suitable only:

- If EHF does not resolve symptoms within 4 weeks and/or
- There is a history of anaphylactic reaction and/or
- Faltering growth in addition to severe GI symptoms
- Reaction to CMP in breast milk and the mother does not wish to continue breastfeeding

AAF	Age group	Cost (correct September 2015)	Notes
First line			
SMA Alfamino [®] (Nestle Health Science)	from birth	400g = £23.00	Please see appendix 1 (p12) for information relating to calcium supplementation.
Nutramigen PURAMINO [®] (Mead Johnson)	from birth	400g = £26.80	
Neocate LCP [®] (Nutricia)	from birth	400g = £28.30	
High calorie AAF			
Neocate Active [®] unflavoured/blackcurrant (Nutricia)	from one year	945g = £66.60	This is a high calorie formula and is not suitable for all infants over 1 year. It is not suitable as a sole source of nutrition.
Neocate Advance [®] unflavoured/banana/vanilla (Nutricia)	from one year	750g = £46.35 1,000g = £58.60	This is a sole source of nutrition for children with CMPA aged 1-10 years. It is a high calorie formula that is not suitable for all infants over 1 year.

Soya Formulae

Soya formula	Notes	Cost (September 2015)
SMA Wysoy®	<ul style="list-style-type: none"> • Should not be prescribed for: <ul style="list-style-type: none"> ○ Infants below 6 months old due to the high phytoestrogen content. ○ Infants with soya allergy and CMPA • Should only be considered for infants with CMPA over 6 months if they are unable to tolerate EHF or AAF, due to the risk of the infant with CMPA developing allergy to soya. • Parents should be advised to purchase soya formula as it is a similar cost to cows' milk formula and is readily available. 	430g = £5.32 860g = £10.15
Alpro Junior 1+ soya milk	from 1 year	Available in supermarkets
Calcium enriched soya/oat milk	from 2 years	Available in supermarkets
Alternative milk suitable for CMPA & lactose Intolerance	Examples of brands (suitable from 2 years)	Cost
Oat milk	Alpro, Oatley,	Available in supermarkets
Coconut milk	Alpro, Koko, Tesco Free From	
Almond milk	Alpro, Tesco Free From	

Formulae and milks that should not be used for CMPA

The following formulae and milks are NOT suitable for infants with CMPA:

- Lactose free formulas: SMA LF[®], Enfamil O-Lac[®]
- Goats' milk
- Sheeps' milk
- Rice milk (unsuitable under age 4 ½ due to arsenic content).

Quantities to prescribe

- Prescribe only 1 or 2 tins initially until compliance/tolerance is established to avoid waste.
- Unless there is anaphylaxis, advise parents to **introduce the new formula gradually** by mixing with the usual formula used in increasing quantities until the transition is complete. Serving in a closed cup or bottle, or with a straw (depending on age) may improve tolerance. Reason: EHF and AAF have an unpleasant taste and smell, which is better tolerated by younger patients (<6 months).
- Note that **stool colour and consistency** may change.
- **Calcium supplementation** may be needed for children over one year depending on volume and type of formula taken. It is rarely required in infants younger than this. The paediatric dietitian will advise.

Age of child	Number of tins for 28 days		
Under 6 months	13 x 400g tins	or	6 x 900g tins
6 – 12 months	7 - 13 x 400g tins	or	3 - 6 x 900g tins
Over 12 months	7 x 400g tins	or	3 x 900g tins
Some children may require larger quantities e.g. faltering growth. Review recent correspondence from the paediatrician or paediatric dietitian			

Amounts based on:

- Infants under 6 months being exclusively formula fed and drinking 150ml/kg/day of a normal concentration.
- Infants 6 - 12 months requiring less formula as solid food intake increases.
- Children over 12 months drinking the 600mls of milk substitute per day recommended by the Department of Health.

Referral to paediatric dietitian and specialist services

Most infants with CMPA can be managed in primary care until weaned.

- **All children with CMPA should be reviewed by a paediatric dietitian to ensure nutritional adequacy of the diet (NICE CG116, 2011).**
- Based on the allergy-focused clinical history, consider referral to secondary or specialist care in any of the following circumstances (NICE guidelines CG116; 2011; Ludman S, et al; 2013):
 - Faltering growth in combination with one or more of the gastrointestinal symptoms mentioned on page 4.
 - Not responded to a single-allergen elimination diet.
 - Had one or more acute systemic reactions.
 - Had one or more severe delayed reactions confirmed IgE-mediated food allergy and concurrent asthma?
 - Significant atopic eczema where multiple or cross-reactive food allergies are suspected by the parent or carer.
 - Persisting parental suspicion of food allergy (especially in children or young people with difficult or perplexing symptoms) despite a lack of supporting history.
 - Diagnostic uncertainty or clinical suspicions of IgE-mediated food allergy but allergy test results are negative.
 - Clinical suspicion of multiple food allergies.
 - Incomplete resolution after cows' milk protein has been excluded.
 - Complex symptoms.

Reviewing and discontinuing treatment

Review prescriptions regularly to check that the formula prescribed is appropriate for the child's age and nutritional requirements.

Avoid adding to the repeat template since quantities required will change with age (see notes above). Refer to recent correspondence from the paediatric dietitian.

Outgrowing CMPA: 60-75% of children with delayed reactions outgrow their cows' milk protein allergy by 2 years of age. This figure rises to 85-90% of children at 3 years of age. Children with immediate allergic reactions to cows' milk tend to outgrow their milk allergy slower with only 50% tolerating cows' milk by their 5th birthday.

Challenging with cows' milk protein: Refer to NICE guidelines (CG116; 2011) regarding which children should be challenged with cow's milk protein in a secondary care setting.

Review the need for the prescription. If you can answer 'yes' to any of the following questions, the child should be reviewed by the paediatric dietitian and/or paediatrician to assess whether cow's milk allergy is still present and formula is still required or if any other supplementation is needed. Please send a new referral or liaise with appropriate services if the child is already under the care of a paediatric dietitian.

- Is the patient over 2 years of age?
- Has the formula been prescribed for more than 1 year?
- Is the patient prescribed more than the suggested quantities of formula according to their age?
- Is the patient able to eat any of the following foods: cows' milk, cheese, yoghurt, ice cream, custard, cakes, chocolate, cream or other foods containing cows' milk

Children with multiple or severe allergies may require prescriptions beyond 2 years. This should always be on the recommendation of the paediatric dietitian.

References and evidence

1. Venter C, Arshad SH (2011). Epidemiology of food allergy. *Pediatr Clin North Am*; 58(2): 327 – 49.
2. Fiocchi A, et al (2010). World Allergy Organisation (WAO) Diagnosis and Rational for action against Cow's Milk Allergy (DRAMCA) guidelines. *Pediatr Allergy immunol; Suppl 21*:1-125.
3. NICE Guidelines, clinical guidelines 116 (2011). Food allergy in children and young people.
4. Vandenplas Y et al (2007). Guidelines for the diagnosis and management of cow's milk protein allergy in infants: *Arch Dis Child*; 92: 902-908.
5. Allen KJ, Davidson GP, Day AS, et al. Management of cows' milk protein allergy in infants and young children: An expert panel perspective. *J Paediatr Child Health* 2009;45:481-8
6. LPP (2013). Paediatric nutritional products Appropriate prescribing resource pack.
7. Ludman S, Shah N, Fox AT (2013). Managing Cow's Milk Allergy in Children. *BMJ*; 347:f5424

Appendix 1:

Quick reference guide to calcium supplementation with amino acid formulae

Please note where an AAF is indicated, the most cost effective and suitable option may depend on whether the infant requires a calcium supplement.

Advice should be given to the parents to ensure the infant follows an appropriate exclusion weaning diet whilst on an amino acid formula. This should include advice on appropriate dietary sources of calcium and whether a supplement is required.

Guidance on calcium supplementation for AAF

Product name	Neocate LCP	Alphamino	Nutramigen Puramino
Formulation	400g tin	400g tin	400g tin
Volume needed to meet RNI for calcium <6months	810mls	930mls	825mls
Amount of Ca ²⁺ from 600mls	393mg	339mg	384mg
Cost per 100kcal	£1.46	£1.14	£1.34

NB – RNI for Calcium in infants 0-12month is 525mg. For children 1-3 years it drops to 350mg.

A calcium supplement may be required for infants taking extensively hydrolysed formulae but dairy alternative products (e.g. soya/oat) may be introduced at weaning to supplement the levels from the formula.

Appendix 2: Quick reference guide to managing infants with cow's milk protein allergy

