This policy statement is approved by Halton, Knowsley, Liverpool, South Sefton, Southport and Formby, St Helens, Warrington, West Lancashire, and Wirral CCGs

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NHS
Pan Mersey
Area Prescribing Committee

LACTOSE INTOLERANCE AND COWS' MILK PROTEIN ALLERGY – Prescribing Guidelines for Specialist Infant Formula Feeds

This guidance outlines recommendations for the prescribing of infant formula feeds in cows' milk protein allergy (CMPA) and lactose intolerance.

GUIDELINE

INTRODUCTION

Cows' milk protein allergy is an immune-mediated allergic response to proteins in milk. It can be immediate in onset following consumption when it is caused by immunoglobulin E antibodies – IgE mediated. When the presentation is delayed by hours or even days following exposure, it is called non-immunoglobulin E mediated or non-IgE mediated reaction.

Lactose intolerance occurs when there is reduced or absence of the enzyme lactase. Lactase is present in the lining of the small intestine. Low levels of this enzyme prevent the effective digestion of lactose sugar and results in loose acidic stools. The undigested lactose sugar arrives into the large intestines where it ferments to produce gas and mild acid that causes discomfort and flatulence.

This guidance covers all infants; including those who breastfeed, who are formula-fed or those who do a combination of both.

The objectives of this guidance are to:

- Aid diagnosis and improve access to special infant formula where needed, minimising distress to the baby and anxiety to the parents/carers.
- Provide guidance on the nature, prescribing and cost effective supply of milk substitutes for babies.
- Provide advice on suitable quantities for prescribing, duration of supply and guidance on stopping prescribing.
- Maintaining awareness that breast milk is considered best for babies and not initiating a change from breast to formula milk if the mother is happy to continue breastfeeding the infant.

This guidance should be used in conjunction with:

- NICE Clinical Guideline 116, Food allergy in children and young people: Diagnosis and assessment of food allergy in children and young people in primary care and community settings,
- NICE Clinical Knowledge Summaries – Cow's milk protein allergy in children (June 2015)

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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EXCLUSION:

Secondary care will lead in prescribing of other specialist infant formula for several special groups of infants such as:

- Pre-term and low birth weight infants (may also require iron and vitamin supplements)
- Disease specific conditions
- Complex IgE and non-IgE mediated food allergies
- Faltering growth
- Complex medical cases
- Cystic fibrosis

and these are outside of the scope of this guidance.

1. KEY MESSAGES

Cows' milk protein allergy:

1.1 Breastfeeding is the best form of nutrition for infants and this should be promoted, supported and protected wherever possible. This includes infants under investigation or with confirmed CMPA.

1.2 Infants requiring specialist milks other than those for lactose intolerance should be managed as per Flow Chart 3, Page 4 - The initial management of cows' milk protein allergy (CMPA) and Flow Chart 4, Page 5 - On-going management of CMPA following exclusion diet. Referrals to infant feeding clinic, dietitian and/or paediatrician should be made in accordance with local pathways.

1.3 Most children with CMPA will have developed some tolerance to cows' milk protein by the age of 1.. Any child still prescribed specialist formula by 2 years of age should be weaned onto supermarket bought milk alternative e.g. calcium enriched soya milk or oat milk. Prescription formula should no longer be required by 2 years.

1.4 Prescribe only enough tins for 1 week initially until compliance/patient acceptability is established to avoid waste.

1.5 Only add infant formulae to the repeat prescribing template in primary care if a review process is established to ensure the correct product and quantity is prescribed for the age of the infant. See Section 7, Page 8 for more detail on quantities to prescribe.

1.6 Soya products should **not** be recommended first line unless advised by a paediatric consultant or dietitian due to the high incidence of soya sensitivity (10-35%) in infants intolerant of cows' milk protein, and never for infants under 6 months of age unless on specialist advice e.g. for galactosaemia. Infants of vegan mothers who choose not to breastfeed should not receive soya formula on the NHS as products are available at the same cost as standard formula.

Lactose intolerance:

1.7 In general, all cases of milk intolerance should be referred for specialist dietetic advice with the exception of simple cases of secondary lactose intolerance, for which a lactose free formula should be advised, and a re-challenge carried out after 8 weeks. If symptoms recur after re-challenge consider referral to general paediatrics.

1.8 Lactose free formula can be bought at an only slightly higher cost to standard infant formula, and prescribers should not routinely prescribe. These have no role in the management of cows' milk allergy. Parents can purchase lactose free formula from their chosen retailer; however they are less commonly used than standard formula and may have to be ordered. Most pharmacies and many supermarkets can obtain stock in a few days.

3. The initial management of cows' milk protein allergy (CMPA)

Delayed onset (Non-IgE-mediated) – generally within 2 – 72 hours (Majority of cases)

One or more of these symptoms (usually non acute)

- Severe colic
- Vomiting
- Reflux
- Bottle refusal or aversion
- Loose or frequent stools
- Perianal redness
- Constipation
- Abdominal discomfort
- Blood / mucus in stools (in an otherwise well infant)
- Pruritus, erythema
- Significant atopic eczema

Signs of faltering growth

Yes

REFER to paediatric consultant and dietician

Formula fed – prescribe **amino acid formula (AAF)**

Exclusively breastfed or mixed-fed

Exclude breastfeeding technique issues

Exclude cows' milk containing foods from maternal diet for 2 – 4 weeks and continue breastfeeding

Prescribe for mother: *Calcichew D3 Forte chewable tablets **2 daily***

Prescribe amino acid formula **(AAF)** for top-up if required.

No

Acute onset (IgE-mediated) – generally within the hour, rarely delayed (Minority of cases)

One or more of these symptoms (usually acute)

- Vomiting
- Diarrhoea
- Abdominal pain / colic
- Acute pruritus, erythema, urticarial
- Angioedema
- Acute 'flare up' of atopic eczema

Signs of faltering growth

REFER to a specialist for a skin prick and/or specific IgE antibody blood test
TREAT as per Box 1, 2 or 3 below whilst waiting for referral appointment.

Anaphylaxis / Severe symptoms

IMMEDIATE A&E REFERRAL

URGENT TREATMENT for

Respiratory cough, wheeze, voice change or breathing difficulty

CVS faint, floppy, pale, collapsed from low blood pressure

URGENTLY TREAT symptoms

IMMEDIATE REFERRAL to specialist

Note: Some infants with CMPA have a mixed – delayed and acute presentation. Treatment should follow the guidance for ***acute*** in these cases.

BOX 1: Formula fed

Trial of **extensively hydrolysed formula (EHF)*** *see section 6.1*

BOX 2: Mixed-fed

Trial of cows' milk free maternal diet with **EHF** top-ups if needed

BOX 3: Exclusively breastfed

Refer to infant feeding lead for breastfeeding assessment prior to prescribing

Exclude cows' milk containing foods from maternal diet for 2 – 4 weeks and continue breastfeeding

Prescribe for mother: *Calcichew D3 Forte chewable tablets **2 daily***

If mothers do not wish to or are unable to follow a milk free diet prescribe **EHF**, If mother is following a milk free diet and symptoms persist, prescribe **amino acid formula** (**AAF)** as top-up if needed

NB Breastmilk may take 1-2 weeks to become truly dairy free from the initiation of maternal exclusion diet.

For formula fed, mixed-fed and exclusively breast fed infants:

Initially prescribe 1 week supply until tolerance reached

Consider referral to community dietitian

If CMPA – most symptoms will settle well within 2 – 4 weeks

**Lactose containing EHF may be more palatable babies over 6 months who don't like the taste of standard EHF lactose-free products.*

4. On-going management of CMPA following EXCLUSION DIET

Delayed onset (Non-IgE-mediated) CMPA

Improves

Perform Home Challenge using cows' milk formula to confirm diagnosis, 2 – 4 weeks after starting Exclusion Diet (click here for example of home challenge)

For weaning, consider home challenge using the 'Milk Ladder'

If symptoms return, CMPA confirmed referral to a dietitian is required.

- continue with **extensively hydrolysed formula (EHF)** in formula / mixed fed infants (**see section 7** for quantity to prescribe)
- exclude cows' milk containing foods from maternal diet again

If symptoms do not return with challenge, CMPA is ruled out.

Not Improved

CMPA still suspected

Refer to paediatric consultant in secondary care

START a trial of amino acid formula (AAF) in formula / mixed fed infants for 4 weeks whilst waiting for referral appointment

NB: Children with enterocolitis/proctitis or blood in stools with faltering growth, severe atopic dermatitis and symptoms during exclusive breastfeeding are more likely to require amino acid based formula.

With support from a dietitian, evaluate the patient every 6 to 12 months to assess whether they have developed a tolerance to cows' milk.

Continue cows' milk free diet until 9 – 12 months of age and for at least 6 months

A **planned REINTRODUCTION** is then required to determine if tolerance has been achieved. iMAP Guideline: The Early Home Reintroduction to Confirm the Diagnosis of Cow's Milk Allergy This can be done using the milk ladder guided by dieticians. Consult paediatric dietician / paediatric consultant for further advice if reintroduction failed.

NB: This involves reintroducing cows' milk into the diet and monitoring of symptoms return. Advise to start with baked milk products (e.g. muffins, cakes and malted milk biscuits) as they are less allergenic. If symptoms return, continue with exclusion diet and evaluate the child after a further 6 to 12 months

NB: Once tolerance is established, gradually encourage less processed milk as advised in the 'Milk Ladder'

Acute onset (IgE-mediated) CMPA

REINTRODUCTION will be managed by secondary care.

NB: GP will provide on-going specialist formula prescription under specialist advice.

5. The management of lactose intolerance

Secondary / acquired lactose intolerance or transient lactase deficiency (Most common problem in infants)

Signs and symptoms of lactose intolerance

- Diarrhoea
- Colic
- Transient nature, usually secondary to GI insult, e.g. post infective
- Diagnosis confirmed by improvement within 2-3 days of starting lactose-free diet
- Resolution within 2-8 weeks

Breast-fed infants:
Refer to infant feeding lead for breastfeeding assessment prior to prescribing*NB: Lactose-free maternal diet is UNNECESSARY as lactose is present in breast milk.*

- **Pan Mersey APC does not recommend prescribing lactase enzyme drops (Colief®) on the NHS but may be purchased (See policy).**
- Encourage mother to continue with breastfeeding to speed up gut healing and provide support as needed through community paediatric dietitian or infant feeding team.

Formula-fed infants:

Temporary switch to a lactose-free formula for a period of 8 weeks after which regular formula can be reintroduced

e.g. SMA LF® or Enfamil O-Lac ® (suitable from birth to max 12 months)

Lactose free formula can be purchased over the counter at a similar price to standard formula and the GP should not prescribe. *Healthy Start vouchers* can be used to purchase lactose free infant formula based on cows' milk

Infants taking solid foods

- Avoid foods containing lactose
- Offer referral to dietitian for dietary advice
- Consider the impact of lactose-containing medicines

Symptoms usually resolve in 2-3 days when lactose is removed from the diet and achievement of this confirms diagnosis. Most children should be able to revert back to normal formula once the gastro-intestinal insult has resolved i.e. within 8 weeks.

- After 8 weeks gradually reintroduce regular formula / breast milk / cows' milk depending on age
- If symptoms return, revisit the diagnosis and consider **referral to a dietitian.**
- Lactose free infant formula should not be used beyond 18 months and infants can be weaned onto proprietary lactose-free cows' milk purchased at supermarkets from 12 months old.

6. Product choice:

All prescriptions for specialist formula should be endorsed '***ACBS***'.

6.1 Extensively hydrolysed formula (EHF)

EHF formula is appropriate for the majority (around 90%) of children with CMPA.
DO NOT prescribe EHF if there is a history of anaphylaxis or severe symptoms.

Product	Age	Presentation/ Cost	Comment
Nutramigen LGG1®	Birth to 6 months	400g tin / £11.21	Nutramigen LGG® and Similac Alimentum® are LACTOSE-FREE. Lactose-free formula may be beneficial if severe GI symptoms / inflammation in GI tract is suspected. ***This MUST NOT be used in infants with lactose intolerance.***
Nutramigen LGG2®	From 6 months	400g tin / £11.21	
Alimentum®	From birth	400g tin / £10.01	
Aptamil Pepti 1®	Birth to 6 months	400g tin / £9.87 800g tin / £19.73	Aptamil Pepti® and Althera® contain lactose and may be more palatable. Althera® is the only EHF suitable for Halal and vegetarian diets
Aptamil Pepti 2®	From 6 months	400g tin / £9.41 800g tin / £18.82	
SMA Althera®	From birth	450g tin / £11.09	
Aptamil Pepti Junior®	From birth	450g tin / £14.33	
Aptamil Pepti Syneo®	From birth	400g tin / £10.65	

Nutramigen LGG 1 and 2® include a probiotic LGG which is purported to accelerate tolerance of cows' milk protein. It is **NOT RECOMMENDED** for premature or immunocompromised infants. The reconstitution guidance is also different to the standard guidance for families at home. Advise family to refer to the product's instruction for details of reconstitution.

Aptamil Pepti Syneo contains Bifidobacterium breve M-16V and is **NOT SUITABLE** for use in premature infants or infants who are immunocompromised. The reconstitution guidance is also different to the standard guidance for families at home. Advise family to refer to the product's instruction for details of reconstitution.

6.2 Amino acid formula (AAF)

Note that these products are almost three times more expensive than EHF and only a small number of infants (around 10%) need to be started on AAF in primary care. They are **suitable** only when

- infant has faltering growth or blood in their stools
- an EHF does not resolve symptoms and / or
- there is evidence of severe (anaphylactic) allergy or
- if the infant remains symptomatic whilst exclusively breast feeding (mother on milk free diet)
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- NB All amino acid formulas are halal, kosher and vegetarian

Product name	Age	Presentation / Cost
EleCare® (Similac)	From birth	400g / £22.98
SMA Alfamino ®	From birth	400g / £22.98
Neocate LCP®	From birth	400g / £22.98
Nutramigen Puramino®	From birth	400g / £22.98
Neocate Syneo®	From birth	400g / £24.82

Neocate Syneo® includes a probiotic (*Bifidobacterium breve*) and plant-based prebiotic. It is **NOT RECOMMENDED** for premature or immunocompromised infants. The reconstitution guidance is also different to the standard guidance for families at home. Advise family to refer to the product's instruction for details of reconstitution.

6.3 Do not prescribe:

- Specific infant formula for lactose intolerance – can be purchased over the counter.
- Soya based formula – not suitable for infants under 6 months old unless advised by specialist. Can be purchased for older infants if parents wish to. Be aware of risk of cross allergy with cows' milk.
  NB: Wysoy® can be used over 6 months of age on specialist advice and can be purchased for the same cost as standard milks and therefore should not be prescribed.
- Colief ® (lactase enzyme), Infacol ® (simethicone) – lack of sufficient evidence to support use in the treatment of symptoms of lactose intolerance or CMPA. See Pan Mersey Policy Statement for Lactase drops.

NB: Sheep or goat's milk is only tolerated by 25% of children with cows' milk protein allergy due to the proteins in them being very similar; therefore, they are not recommended.

7. Quantities to prescribe:

To avoid waste, initially prescribe maximum of 1 week supply in case there are palatability issues or until tolerance/compliance is established.

Age of child	Average total volume feed per day (estimated)	No of tins required for 28 days complete nutrition	Department of Health recommendations (based on average weight for age)
Under 6 months	1000mls	10 x 400g (or 450g)	Exclusively formula fed based on 150mls/kg/day of a normal concentrated formula
6 – 9 months	800mls	8 x 400g (or 450g)	Requiring less formula with increased weaning and solid intake
9 – 12 months	600mls	6 x 400g (or 450g)	
Over 12 months – dietitian review for continued need for formula	600mls	6 x 400g (or 450g)	Requiring 600mls of milk or milk substitute per day

NB: Some children may require more e.g. those with faltering growth. This table provides guidance only. Follow advice of specialist or dietitian.

8. Review and discontinuation of specialist formula

- Infants with confirmed non-IgE CMPA should be referred to a community paediatric dietitian.
- Ensure there is a clear formula prescribing monitoring plan is in place. The paediatric community dietitian or paediatrician should give clear guidance about how long specialist formula is required for. Add this review date to repeat prescription template. Review regularly against quantities and type of formula prescribed and child's increasing age. Ensure infant's growth is monitored and recorded.
- Review the prescription for all existing patients if:

- The patient is over 2 years old – refer back to community paediatric dietitian unless advised that special formula is still required by dietitian.
- The quantity of formula prescribed is higher than recommended according to their age – refer back to community paediatric dietitian.
- The patient tolerates cows' milk – stop the prescription.

NB: Children with multiple or severe allergies may require prescriptions beyond two years. This should always be at the suggestion of the paediatric dietitian.

9. Practical advice:

- It is often difficult to wean babies from breast feeds to formula feeds for various reasons.
- EHF is the appropriate choice for vast majority of infants with CMPA.
- Try a formula for a minimum of 2-4 weeks.
- 2 to 4 weeks without allergen should improve symptoms.
- Both EHF and AAF are less palatable than the standard infant formula bought over the counter and are often initially rejected by infants over 6 months.
- If an infant does not tolerate taste suggest titrating with regular formula (not for infants with history of anaphylaxis or severe symptoms). However, direct switch to formula will eliminate allergen sooner.
- Infant stools may change and have a green tinge. This is seen with both EHF and AAF and is not clinically relevant.
- If the infant is not thriving, review treatment. Only around 10% of infants on EHF will not tolerate this type of formula and subsequently have persistent CMPA symptoms and faltering growth (due to residual allergen contents). Seek advice of community paediatric dietitian or general paediatrician.
- Parents can be advised to keep a diary of symptoms and include photographs that may aid diagnosis.
- Parents need advice on cows' milk free weaning diet as appropriate. The process of tolerance development is dynamic and a dietitian should evaluate these infants and direct parents on milk reintroduction on a case by case basis.
- Some formulas have higher sugar content. Ensure dental hygiene advice given.
- Do no start formula in children over 1y old, advise to buy a calcium fortified milk alternative such as soya or oat milk.

Useful Information:

1. Parent information – Cows' milk allergy (produced by North West Paediatric Allergy Network)

Reference:

1. Diagnosis and management of non-IgE mediated cows' milk allergy in Infancy - a UK primary care practical guide Carina Venter, Trevor Brown, Neil Shah, Joanne Walsh, Adam Fox www.ctajournal.com/3/1/23 2013
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4. National Institute of Health and Clinical Excellence. Food allergy in children and young people. Diagnosis and assessment of food allergy in children and young people in primary care and community setting. NICE Clinical Guideline 116, February 2011. Accessed 08/12/2020.
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9. NICE Clinical Knowledge Summaries – Cow's milk protein allergy in children (June 2015) Accessed 21/03/2017
10. The International Milk Allergy in Primary Care (iMAP) Guideline 2019 (accessed 08/12/2020) https://gpifn.org.uk/imap/
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15. Greater Manchester Shared Services – Prescribing infant formula for cow's milk protein allergy in primary care (May 2016)