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

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PAN MERSEY APC

NHS
Pan Mersey
Area Prescribing Committee

Pan-Mersey Prescribing Guidelines for Specialist Infant Formula Feeds in Lactose Intolerance and Cows' Milk Protein Allergy

With acknowledgement to North West Paediatric Allergy Netwrok, Alder Hey Children's NHS Foundation Trust

Ref: G16 FINAL Version:2.0
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(or earlier if there is significant new evidence relating to this recommendation)

1. 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.

Food allergy should not be confused with food intolerance, which is a non-immunological reaction that can be caused by enzyme deficiencies, pharmacological agents and naturally occurring substances.

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 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.

The purpose of this guidance is to outline recommendations for the prescribing of infant formula feeds in cows' milk protein allergy (CMPA) and lactose intolerance in the Pan-Mersey area.

This guidance covers all infants; including those who breastfeed, who are formula-fed or those who do a combination of both. For breast-fed babies who present with cows' milk protein allergy, breastfeeding should be protected as this is usually the best management. Specialist milks should only be considered when there is truly a clinical need after thorough assessment. Assessment should include and consider whether formula feed products are being correctly prepared. 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)

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 food intolerances and allergies
- Faltering growth
- Complex medical cases
- Cystic fibrosis

and these are outside of the scope of this guidance.

2. KEY MESSAGES

Cows' milk protein allergy:

2.1 Breastfeeding is the best form of nutrition for infants and this should be promoted, supported and protected wherever possible.

2.2 Powdered milks should be the norm. Liquid feeds are a convenience product and should be purchased if preferred, unless they are clinically indicated by a dietician or specialist.

2.3 Infants requiring specialist milks other than those for lactose intolerance should be referred to a dietitian or paediatric consultant for IgE-mediated allergy. Prescribing can be initiated in primary care in the short-term whilst waiting for specialist referral. If longer-term use is required dietician/specialist opinion must be sought and there should be a clear plan for weaning and discontinuation included in the care plan from the dietician/specialist. In the absence of written guidance to the contrary, the recommended maximum ages detailed in this guidance should be applied.

2.4 Most children with CMPA will tolerate normal milk at the age of 1. Any child still prescribed specialist formula by 2 years of age should be weaned onto supermarket bought milk e.g. calcium enriched soya milk. Prescription formula should no longer be required by 2 years 6 months.

2.5 Prescribe only one or two tins initially until compliance/patient acceptability is established to avoid waste.

2.6 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.

2.7 Soya products should **not** be recommended for purchase 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.

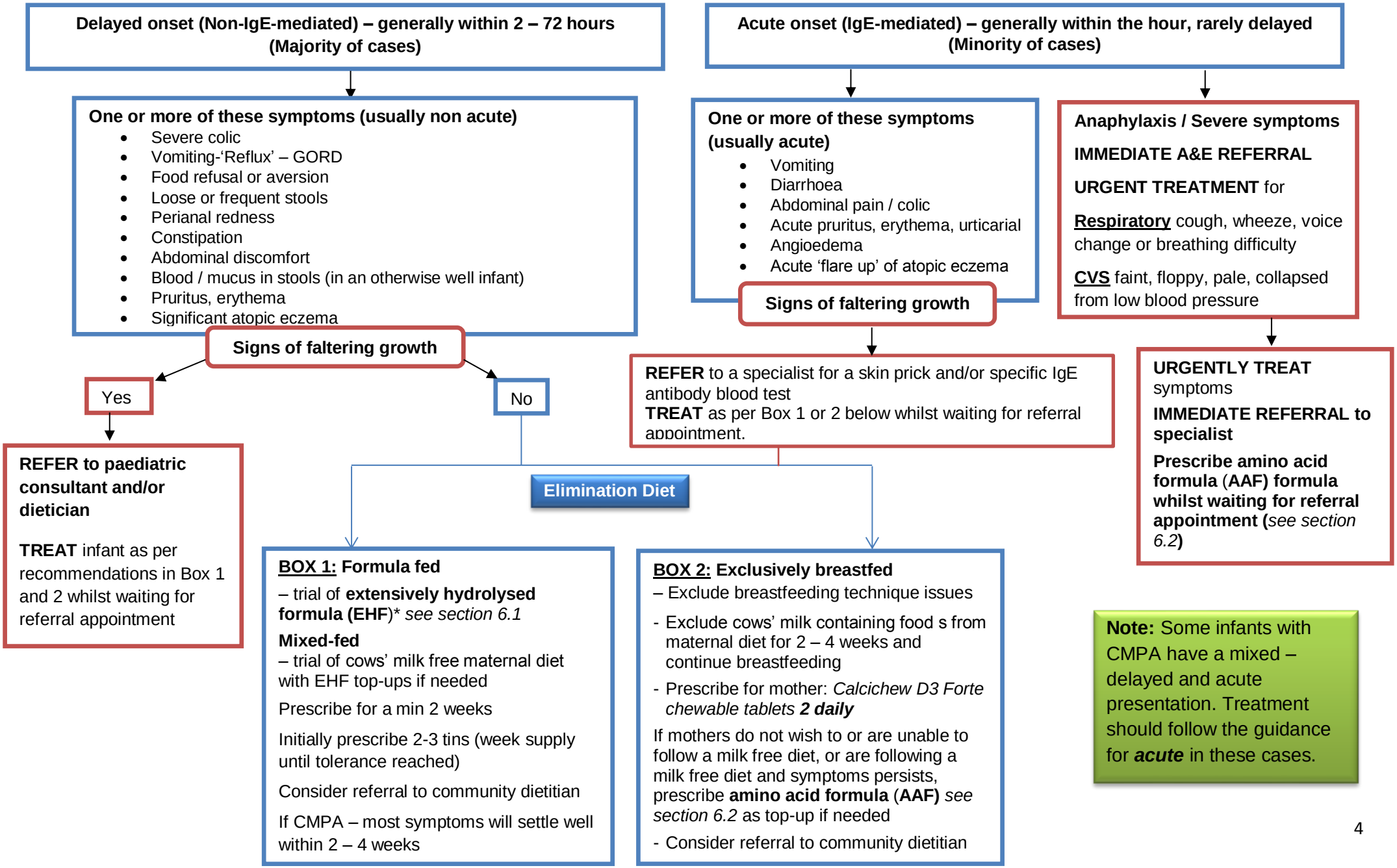
Lactose intolerance:

2.8 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 in 4 to 8 weeks. Lactose intolerance is due to enzyme deficiency; it is not an allergy**.**

2.9 Lactose free milks can be bought at a only slightly higher cost to standard infant formula, and prescribers should not routinely prescribe. These have no role in the management of cow's 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.

2.10 Do not prescribe low lactose/lactose free formulae in children with secondary lactose intolerance over one year old who previously tolerated cows' milk, since they can use lactose free products (e.g. Lactofree®) from supermarket.

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



Lactose containing EHF may be more palatable if the baby doesn't like the taste of standard lactose-free products.

4. On-going management of CMPA following ELIMINATION DIET

Delayed onset (Non-IgE-mediated) CMPA

Improves

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

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

If symptoms return, CMPA confirmed

- continue with **extensively hydrolysed formula (EHF)** in formula / mixed fed infants (**see section 7** for quantity to prescribe)
- exclude cow's 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.

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 – with support of dietitian

A **planned REINTRODUCTION** is then required to determine if tolerance has been achieved. 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 elimination 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

Improves

Do Not Home Challenge after 2 – 4 weeks and continue with elimination diet

Secondary care will continue with on-going follow ups.

Not Improved

CMPA still suspected

Refer to paediatric consultant in secondary care

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 two weeks

Breast-fed infants:

- Exclude breastfeeding technique issues

NB: Lactose-free maternal diet is UNNECESSARY as lactose is present in breast milk.

Mild symptoms:

- **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

Severe symptoms:

- Consider alternative feeding option temporarily whilst continue to express breast milk to maintain supply
- Consider advising parents purchase lactose free formula feed
- Seek specialist advice e.g. health visitor / breastfeeding advisor

Formula-fed infants:

Temporary switch to a lactose-free formula for a period of 4 - 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 solids 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 6-8 weeks.

- Gradually reintroduce regular formula / breast milk / cows' milk 4 to 8 weeks later depending on age
- For infant started on solids, reintroduce cows' milk containing food gradually.
- Sometimes, symptoms may last 3 – 6 months. If longer term, use lactose-free formula as necessary and **refer to dietitian and/or paediatric consultant**.
- Lactose free infant formula should not be used beyond 18 months and infants can be weaned onto proprietary lactose-free milks purchased at supermarkets from 12 months old.
- If re-challenge fails, revisit the diagnosis and if necessary **refer to a dietitian** explaining reasons.

PRIMARY lactose intolerance is due to lactase enzyme deficiency, not an allergy. It is a genetic disorder and usually presents in later childhood or adult life.

Referral should be made to a paediatric consultant and dietitian for all suspected primary lactose intolerance where there is significant weight loss or no improvement after withdrawal of lactose.

Long term need for a lactose-free diet requires dietetic referral

6. Product choice:

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 / £10.99	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 / £10.99	
Similac Alimentum®	From birth	400g tin / £9.10	
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
Aptamil Pepti 2®	From 6 months	400g tin / £9.41 800g tin / £18.82	
Althera®	From birth	450g tin / £11	

Nutramigen LGG 1 and 2® have undergone some changes in the past year and it now includes 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.

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

- 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).

Product name	Age	Presentation / Cost
Alfamino ®	From birth	400g / £23
Neocate LCP®	From birth	400g / £28
Nutramigen Puramino®	From birth	400g / £27

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

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.
- Flavoured products – no clinical advantage
- Liquid ready to feed products – no clinical advantage, may be more palatable and useful if concerns over making up powdered formula

- 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.
- Nutriprem® in primary care to promote weight gain in term infants

NB: Sheep or goats milk may be tolerated by approximately 25% of children with cows' milk protein intolerance. However as the proteins in sheep or goats milk are similar to cows' milk, most infants will also react to these and so they are not normally recommended.

7. Quantities to prescribe:
To avoid waste, initially prescribe maximum of 1 week supply (2 – 3 tins) 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
- Ensure formula prescribing is monitored. If no robust monitoring in place do not prescribe formulas on repeat template. If applicable add review date to prescription
- Review regularly against quantities and type of formula prescribed and child's increasing age. Ensure infant's growth is monitored and recorded.
- Review against recent correspondence from specialist, if applicable (e.g. children with higher nutritional requirements or multiple allergies may need more formula for a longer period of time).
- Review the prescription for all existing patients if:
  - The patient is over 2 years old
  - On formula for more than a year
  - The quantity of formula prescribed is higher than recommended according to their age
  - The patient can eat/drink cows' milk containing food (e.g. cows' milk, yoghurt, cream, butter, cheese, ice-cream, custard, chocolate, cakes, margarine, ghee).

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 two weeks and avoid product switching
- 2 to 6 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
- 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
- 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 dietitian
- Immediate need to prescribe AAF happens rarely. Only prescribe AAF when infant has a history of anaphylaxis, and/or has very severe symptoms. Note that majority of these infants can be changed to EHF at a later date with risk assessment / challenge by a specialist. This consideration is an important step as there is emerging evidence that tolerance to cows' milk occurs sooner on sustained exposure to extensively hydrolysed formulas
- Parents can be advised to keep a diary inclusive of symptoms and 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 not start formula in children over 1 year old

Useful Information:

1. Parent information leaflet – 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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