



County Durham & Tees Valley
Area Prescribing Committee



North Yorkshire & York Area
Prescribing Committee

Guidelines for recognition and management of non- IgE cow's milk allergy in children

This pathway is intended for use by both primary and secondary care

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Version 1

We promote breast feeding as the best form of nutrition for infants and this should be promoted and supported wherever possible. Almost all children with cow's milk allergy can continue to be successfully breast-fed with modification of mother's diet under the direction of a dietitian.

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Conflict of Interest Statements Dec 2021

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Principal investigator for NIHR Aptamil Pepti Syneo trial (product with Pre/probiotics) trial, recruited patients in the year 2019/2020. There are no other additional conflicts of interest.

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Participated in NIHR Aptamil Pepti Syneo trial and recruited patients for this trial in the year 2019/2020. There are no additional conflicts of interest

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No conflict of interest declared

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No personal conflict of interest. Harrogate trust has a contract with Abbot and prescribes their products as first-line milk.

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No conflict of interest

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Introduction:

This guideline has been developed to aid primary and secondary care health professionals (doctors, dietitians, health visitors and other supporting professionals) in the diagnosis and management of infants and young children with non-IgE cows' milk protein allergy (Non-IgE CMA) at the point at which they present. Most cases of non-IgE CMA should be treated in primary care with appropriate dietetic support. Infant's growth and the need for formula should be monitored regularly by the prescriber.

This guideline is consistent with the [international Milk Allergy in Primary Care \(iMAP\) guidelines](#) ⁽¹⁾ and [NICE pathway](#) ⁽²⁾ and provides recommendation on the presentation, diagnosis and management of Non-IgE CMA in primary care.

Aims and objectives:

- To provide a consistent approach to the management of Non-IgE CMA and discuss alternative pathologies which may mimic non-IgE mediated milk allergy- this pathway does not deal with IgE mediated cow's milk allergy.
- To provide evidence based support for diagnosis and management using the NICE Clinical pathway on CMA and iMAP Guidelines (management of milk allergy in primary care)
- To provide a clear and concise description of formula milks that are suitable for the treatment of infants with non-IgE mediated milk allergy (in those not breastfeeding)
- To provide/signpost primary and secondary healthcare providers with resources to support parents/carers at the time of diagnosis of CMA.

Background

Cows' milk protein allergy (CMA) may be defined as reproducible immune mediated allergic response to one or more proteins in cow's milk ^(2, 3). CMA typically presents in the first year of life and the estimated population prevalence varies between 1.8% and 7.5% of Infants during the 1st year of life ⁽³⁾. Recent population based EuroPREVALL study done in Europe (Challenge Proven CMA) reports a prevalence of < 1% in children up to age 2 ⁽⁴⁾. Symptoms commonly presents in infancy and most affected children present with symptoms by 6 months of age. Onset is rare after 12 months.

CMA can be classified into either immediate onset or delayed onset according to the timing of symptoms and organ involvement (See [Table 1](#) for details). Most have symptoms that fall into mild to moderate clinical expression of non-CMA and most then remain within primary care for the diagnosis and management. Most children outgrow immunoglobulin E (IgE) mediated milk allergy by 5-6 years, non-IgE CMA is usually outgrown much sooner ⁽³⁾. Our clinical practise suggests that most outgrow Non-IgE Milk allergy by 18mths - 2 years of age.

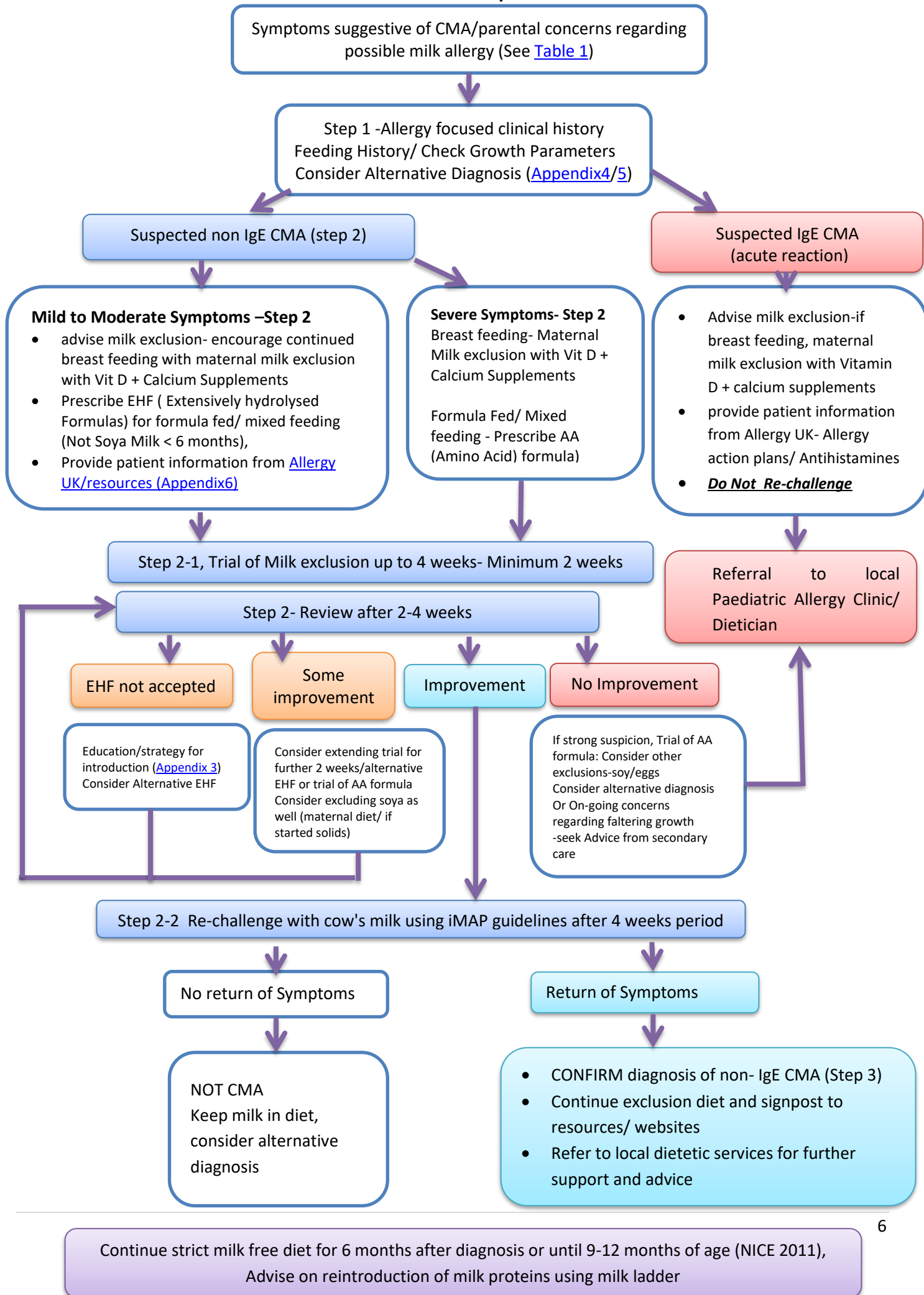
Symptoms of Non-IgE CMA:

Allergy to cow's milk protein should be suspected in infants who present with any of the symptoms listed in the following table ([Table 1](#)), in association with the introduction of cow's milk into their diet.

Table 1 – Signs and Symptoms of CMA (Cow's Milk Allergy)¹

	Mild-moderate non-IgE CMA	Severe non-IgE CMA	IgE CMA
Timing and presentation	<p>Mostly 2-72 hours after ingestion of cow's milk protein (CMP) Formula fed, exclusively breast-fed or at the onset of mixed feeding</p> <p>Treatment resistance-eg atopic dermatitis or reflux, increases the likelihood of allergy</p>	<p>Mostly 2-72 hours after ingestion of cow's milk protein (CMP) Mostly formula fed, exclusively breast-fed or at the onset of mixed feeding</p> <p>Treatment resistance eg atopic dermatitis or reflux, increases the likelihood of allergy</p>	<p>Mostly within minutes (maybe up to 2 hours) after ingestion of cow's milk protein (CMP)</p> <p>Mostly formula fed or at the onset of mixed feeding</p>
Signs and Symptoms	<p><i>(Usually several of the following symptoms)</i></p> <p>Gastrointestinal:</p> <ul style="list-style-type: none"> • Irritability – colic • Vomiting – reflux – GORD • Food refusal or aversion • Diarrhoea like stools – loose and or more frequent • Constipation – especially soft stools with excessive straining, abdominal discomfort, painful flutters • Blood and/or mucus in stool in otherwise well infant <p>Skin:</p> <ul style="list-style-type: none"> • Pruritus (itching) • Erythema(flushing) • Nonspecific rashes • Moderate persistent atopic dermatitis 	<p><i>(Severe persisting symptoms of one or more of the following)</i></p> <p>Gastrointestinal:</p> <ul style="list-style-type: none"> • Diarrhoea, • Vomiting • Abdominal pain • Food refusal or aversion • Significant blood or mucus in stools • Irregular or uncomfortable stools +/-faltering growth <p>Skin:</p> <ul style="list-style-type: none"> • Severe atopic dermatitis +/-faltering growth 	<p><i>(One or more of the following symptoms)</i></p> <p>Gastrointestinal</p> <ul style="list-style-type: none"> • Acute vomiting or diarrhoea, abdominal pain/colic. <p>Skin:</p> <ul style="list-style-type: none"> • Acute pruritus, erythema urticaria angioedema • Acute flaring of persisting atopic dermatitis • Acute worsening of eczema, <p>Respiratory:</p> <ul style="list-style-type: none"> • acute rhinitis +/- conjunctivitis <p>Anaphylaxis</p> <ul style="list-style-type: none"> • Severe IgE mediated cow's milk allergy
Actions	<ul style="list-style-type: none"> • Elimination diet (2-4 weeks) followed by a planned reintroduction challenge (See Algorithm) • This is to check whether symptoms recur and confirm diagnosis. (This may not be appropriate in all cases) • If diagnosis confirmed, refer to Dietitian for CMP exclusion diet advice –Continue breast feeding as far as possible with maternal milk exclusion • If symptoms are well controlled – No need to refer to a paediatrician 	<ul style="list-style-type: none"> • Initiate Elimination diet (2-4 weeks) and review (See Algorithm) • Urgent dietetic referral if concerns regarding growth • Consider referral to Paediatrician with a special interest in allergy if additional concerns 	<ul style="list-style-type: none"> • Refer to Dietitian for cow's milk exclusion advice. • Refer to a paediatrician with a special interest in allergy for testing (Skin Prick Testing/ Specific Ige) and management. • NICE food allergy guideline states children with IgE allergy must not be challenged in the community • Recommend cow's milk replacement – extensively hydrolysed formula as the 1st line for mild to moderate IgE mediated CMA and amino acid formulas for severe CMA

CMA Pathway



STEP 1 – Assess likelihood of IgE or non-IgE-mediated allergy

- An **allergy-focused clinical history** is the cornerstone of the diagnosis.
- A family history of eczema, asthma, hay fever, allergic rhinitis or food allergy is more likely in IgE-mediated food allergy.
- Feeding history – check the source of cows' milk e.g. is the infant breastmilk/formula fed or weaned onto solids.
- Ask about **age** of first onset, **speed** of onset and **severity** following milk ingestion (IgE/ Non IgE CMA- [See Table 1](#)). Also ask about previous management including medication use and response. Rule out other alternative diagnosis/ milk related conditions ([Appendix 4](#), [Appendix 5](#))
- Weigh and measure the child to assess growth.
- Examine the child to check for signs of allergy related comorbidities e.g. atopic eczema, wheeze
- Discourage parents / carers from seeking advice from unregulated alternative allergy practitioners.

STEP 2 – Confirming diagnosis and manage Non-IgE-mediated cows' milk protein allergy

1. Advise a trial elimination of cows' milk for a period of 2-4 weeks ⁽⁵⁻⁷⁾:

- Healthcare professionals should encourage and support breast feeding, in line with the WHO Guidelines and be aware of the negative psychological effect of elimination diet
- Elimination of cow's milk protein in maternal diet should be recommended as the 1st option for breast feeding infant with appropriate nutritional advice for mothers. Elimination should be suggested only if baby symptomatic on breast feeds. For formula fed, Milk free options should be prescribed ([See Appendix 1/2](#))
- Verbal *and* written advice should be provided on the avoidance of food containing cows' milk protein. Patient information sheets are available from Allergy UK, British Dietetic Association ([Appendix 5/6](#))
- If symptoms do not improve (and exclusion has been adhered to) then it is not CMA, consider alternative diagnosis.
- If symptoms improve on exclusion, then CMA is likely, but a re-challenge is essential to confirm diagnosis (especially if other treatment options have been started concurrently). As cow milk free diet has significant impact on dietary restriction, re-challenge is an important step in diagnosis
- See [step 3](#) and [appendix 1](#) for exclusion and replacement advice; consider both maternal & infant diet when providing this advice.
- Consider additional soya exclusion if remains symptomatic, consider egg exclusion if severe eczema and seek advice from paediatric dietician.

2. Re-challenge to confirm the diagnosis of Non-IgE-mediated cows' milk protein allergy (after 4-6 week exclusion)⁵⁻⁷

- Explain to parents why the reintroduction phase is essential.
- If the infant is exclusively breastfed introduce cows' milk back into the diet of the mother.
- If the child is formula or mixed-fed reintroduce cows' milk formula. The iMAP guide on re-challenging (Home introduction –Protocol- [Appendix 6](#)) with CMA gives parents a structured approach to formula reintroduction.
- If the child has been weaned onto solid foods, then introduce cow's milk into the diet and return to cow's milk based formula
- If symptoms do not return then the diagnosis is not CMA, or the CMA has been outgrown.
- If symptoms return with the challenge, confirm the diagnosis of Non IgE CMA, then return the child to a strict CMA free diet
- Those with severe Non IgE CMA and complicated path to diagnosis and ultimately require an amino acid Formula, a delay re-challenge process can be considered until 1 year of age assuming symptoms have satisfactorily resolved.

Table 2: General recommendations for Cow's milk free diet (See [Appendix 1](#) for the Formulary) ^(2,5, 6, 7, 8)

Exclusively breast-fed	Formula +/-breast-fed	Taking solids
<ul style="list-style-type: none"> If an exclusively breastfed infant/ child is symptomatic, advise mother to exclude cows' milk protein from her diet. A maternal milk substitute should be advised. If symptoms only on introduction of cow's milk in weaning / cow's milk feed encourage and support return to breast feeding. Mother can continue to consume cow's milk containing foods in her diet For infants with severe eczema, cow's milk and egg free diet is recommended if poor response to milk free diet and eczema management strategies 	<ul style="list-style-type: none"> Advice on the replacement of cows' milk based formulas with extensively hydrolysed formulas (EHF) as first line. For mixed fed infants, if symptoms occur only with the introduction of top-up formula feeds, replace these with EHF top-ups. The mother can continue to consume foods containing cows' milk protein For mixed feeding refer mother to local specialist/additional breastfeeding support with return to exclusive breastfeeding or increased breastmilk if this is mother's choice 	<ul style="list-style-type: none"> Advise parents/carers to exclude cows' milk protein from the child's diet. Advise on a suitable milk alternative-EHF is usually preferred, although soya formula can also be used after 6 months Introduce milk free solids no earlier than 17 weeks.
<p>Breastfeeding is supported as the best form of nutrition for a good start in life for every child</p> <ul style="list-style-type: none"> In a small number of exclusively breastfed infants, CMA can develop, as cow's milk proteins from the mother's diet can pass into breast milk. These infants tend to be some of the most allergic and are more likely to suffer from multiple food allergies. Breast feeding mothers have calcium requirements of 1000mg/ day and 10mcg (400 IU) vitamin D daily and should be advised supplementation 		

Table 3 – Suggested Monthly Milk free prescribing amounts

Initial prescription should be 2-4 tins until compliance / tolerance is established to avoid waste. Review in 1- 2 weeks (if possible) or issue a second prescription with enough to last 1 month if baby tolerates milk formula and review at 4-6 weeks to discuss improvement and support re-challenge if appropriate

- Some children may require larger quantities e.g. faltering growth.
- Amounts might vary slightly with large size and stage of weaning

Age	General Advice	Formula Quantity/ month
< 6 months	Infants under 6 months being exclusively formula fed and drinking 150ml/kg/day of a normal concentration formula.	10-13 x400 g Or 5-6 x 400 g every 2 weeks
6-12 months	Infants 6-12 months requiring less formula as solid food intake increases.	7-13x 400 g
12 months plus	Small proportion of milk allergic children will require on-going prescription	Approx. 7 x400g- Prescribe based on needs

Hypoallergenic milks in the treatment of CMA

Extensively Hydrolysed Formula (EHF)

This type of formula is based on cows' milk protein and is either whey or casein based. The proteins have been extensively hydrolysed so that they are not recognised by the immune system and therefore will not trigger an allergic reaction in most infants. These milks are recommended as a **first line treatment** in most cases. Patients unresponsive or partially responsive to a trial of two different EHF's can be progressed to Amino Acid Formula (AAF). At least 90% of children with proven CMPA should tolerate these feeds ^(6,7)

Amino Acid based Formula (AAF)

This type of formula contains 100% free amino acids and is considered to be non-allergenic. Only 10% of Infants with Non-IgE CMA should require management with AAF ^(6,7). **These milks are recommended as second line treatment but may be used as a first line treatment in a small number of clinical cases if there are:**

- Severe symptoms of non- CMA associated with faltering growth/weight loss
- Significant blood in stools associated with other gut symptoms/ GORD/ faltering growth
- Milk allergy highly suspected-poor response to EHF/ Maternal cow's milk exclusion (after 4 weeks trial)
- Early onset Severe eczema- Poor response to EHF trial
- Multiple food allergies

Ongoing prescription of specialised formula

- All infants requiring hypoallergenic formula will continue to require monthly repeat prescriptions until at least 6 months after diagnosis. Do not routinely prescribe milk free formula for children over 18 months of age unless recommended by dietitian or paediatrician.
- Quantities of formula required will change with age – see guide to quantities required ([Table 3](#)).
- Prescriptions should be stopped when the child has outgrown the allergy. According to the latest European data, 57 to 69% of infants with CMPA are able to tolerate cow's milk 12 months after initial reaction. ⁽⁴⁾

Review the need for the prescription if you can answer 'yes' to any of the following questions:

- Is the patient over 18 months of age?
- Has the formula been prescribed for more than one year?
- Is the patient prescribed more than the suggested quantities of formula according to their age?
- Is the patient prescribed a formula for CMPA but able to eat any of the following foods – cow's milk, cheese, yogurt, ice-cream, custard, chocolate, cake, butter, margarine, ghee?
- Children with multiple or severe allergies may require prescriptions beyond this time period- This should always be at the suggestion of the paediatric team.

Milk alternatives

- Soya formulas (Wysoy®/ Infasoy) is not recommended for the treatment of CMA in infants < 6 months due to the high content of phyto – oestrogen content of milk ^(9,10). From 6 months of age, soya formulas can be used in the treatment of CMA/Lactose intolerance where soy is being considered/ used in weaning diet. It could also be considered in infants who do not tolerate first-line EHF. There is also potential risk of cross reactivity to soya protein when used in the treatment of Cow's Milk Protein Allergy of approximately 25-60% in Non IgE CMA ⁽⁸⁾.
- Other milk free alternatives include Oat Milk, Pea Milk, Coconut milk, Almond Milk, Hemp Milk which can be used with cooking from 6 months onwards and as a Milk Substitute from 1 year of age (Calcium and iodine enriched)
- Rice milk is not suitable for children under five years due to its arsenic content.
- Lactose free formulae (SMA LF®) are not suitable for those with CMA.
- Other mammalian milk proteins (including unmodified cow, sheep, buffalo, donkey, camel, horse, or goats' milk/formula) are not recommended for infants with cows' milk protein allergy. Most are not adequately nutritious to provide the sole food source for infants and there is a risk of allergenic cross-reactivity with cows' milk.

STEP 3: Ongoing Management of Non IgE CMA ^(5,6,7,8)

- Strict avoidance of cows' milk protein for at least 6 months after diagnosis or until the child developmentally able to manage the foods of milk ladders. This is likely around 9 months and milk introduction should not be delayed beyond 12 months (especially if they have been milk free for > 6 months)
- Some of the Milk free formulas have a thinner consistency and if on-going reflux symptoms consider Instant Carobel (OTC) / Gavison to help with reflux ([Appendix 5](#))
- Information about achieving Milk free diet with adequate calcium/ Vitamin D requirements can be provided from the BDA, Allergy UK ([Appendix 6](#), [Appendix 7](#))
- Following milk free diet, advise a planned home re- introduction of cow's milk into the mothers or infants diet to assess if tolerance has been acquired
- In infants with a strong personal/ family history of atopy however, particularly those with moderate to severe eczema, an IgE sensitisation test to CM should be considered, to ensure that their allergy has not evolved into IgE mediated allergy following an extended period of complete CM avoidance³. In these children, do not advise Home introduction and instead arrange a referral to an allergy clinic.
- Challenge as per milk ladder which has all the relevant advice about reintroduction (iMAP milk ladder- [Appendix 6](#))
- If failed on milk challenge step, family to re-challenge child every 2- 3 months to check resolution / development of tolerance. If symptoms recur, continue cows' milk avoidance management.

STEP 4- When to refer:

Refer to paediatric dietetic service:

- Every child with CMA should be signposted to resources/ have access to dietitian.
- If there is concern about the nutritional adequacy of the child's diet and faltering growth across 2 centiles on a milk free diet, refer to paediatric dietitian.
- Referral criteria and access to community/specialist support vary across region. Please follow local pathway.

Refer to paediatric allergy service:

Patients who present with, or develop any of the following symptoms/situations during primary care management:

- A clinical history strongly suggestive of IgE-mediated cows' milk allergy (with positive or negative allergy tests)
- An acute systemic reaction involving wheezing, difficulty breathing, drowsiness, loss of consciousness or a severe delayed reaction
- A history of reacting to other foods (multiple Mixed/ IgE food allergies)
- Faltering growth, especially in combination with any gastro-intestinal symptoms
- Other co- morbidities : recurrent wheeze, moderate to severe eczema, severe reflux symptoms etc
- If symptoms do not respond to exclusion of cows' milk
- Persisting parental/carer suspicion of food allergy or concern once primary care measures have been tried.

Appendix 1: Hypoallergenic milk formulas ⁽⁵⁾

Choice of formula within each group should not be dependent on the cost of formula alone; additional benefits seen with formulas incorporating a prebiotic or probiotic can include a more rapid resolution of symptoms and a reduced likelihood of developing other atopic problems in the future. If a baby does not settle on one EHF they may settle with another EHF with a different base. Paediatric dietitians in each ICS are happy to offer advice about choice of EHF.

Extensively Hydrolysed Formulas (eHF)		
First line and alternative eHF	Age Range	Notes
Althera® (450g) (Nestle)	Birth to 3 years	Whey based, contains lactose, medium chain triglycerides (MCT), more palatable for infants who have started weaning.
Aptamil Pepti 1® (400g/800g) Aptamil Pepti 2® (400g/800g) (Danone Nutricia)	Birth to 6 months 6 months – 2 years	Whey based, contains lactose (3.8g per 100mls), more palatable for infants who have started weaning Contains prebiotic oligosaccharides (9:1 blend of Galacto- and Fructo-oligosaccharides(GOS/FOS) (Least level of Hydrolysis of Milk protein)
*Nutramigen 1 with LGG® (400g) *Nutramigen 2 with LGG® (400g) (Mead Johnson)	Birth to 6 months 6 months to 2 years	Casein based, Lactose free Note: preparation instructions differ to other milk formulas. Contains LGG(Lactobacillus Rhamosus) probiotics -Clinically proven to accelerate return to cow's milk and reduce risk of other allergic manifestations- <i>Not suitable for premature or immunocompromised infants</i>
*Similac Alimentum® (400g) (Abbott) *Currently Product recalled as of 11/03/2022	Birth to 2 years	Casein based, lactose content < 10mg/100 mls, Contains 33% MCT Contains prebiotic (2'-FL HMO-Human Milk Oligosaccharide)- proven benefit for the gut bacteria and can affect systemic immune responses
Notes		
<ul style="list-style-type: none"> If first line formula is not tolerated/accepted, STOP and then trial an alternative EHF. For infants with severe diarrhoea trial lactose free eHF first line. Nutramigen 1 & 2 with LGG® and Neonate Syneo® should be prepared with boiled water cooled down to room temperature (not 70°C). Note: This is currently not in line with DOH guidance on safe preparation of infant formula and parents should be made aware of the risk of infection. Consider AAF if trial of two different EHF products have not been tolerated. 		
Amino Acid Formula (AAF) for severe CMPA		
DO NOT INITIATE IN PRIMARY CARE UNLESS SEVERE CMPA unresponsive or partially responsive to Ehf (See Criteria for AAF)		
Amino Acid Formula	Age Range	Notes
SMA Alfamino® (400g) (Nestle)	Birth to 3 years	Contains 24.4% MCT
Neocate Infant® (400g) (Nutricia)	Birth to 12 months	MCT 33%, Has added Nucleotides & DHA/ARA, (Docosahexanoic acid (DHA). Arachidonic Acid(ARA)
Nutramigen Puramino® (400g) (Mead Johnson)	Birth to 2 years	Contains 33% MCT
Elecare (Abbott) *Currently product recalled as of 11/03/2022	From Birth	33% MCT, Contains prebiotic (2'-FL HMO-Human Milk Oligosaccharide)- proven benefit for the gut bacteria and can affect systemic immune responses
Neocate Syneo® (400g) (Nutricia)	From birth	Amino acid formula with pre- and probiotics(HMO, DHA/ARA and Bifidobacterium Breve) <i>Not suitable for premature or immunocompromised infants.</i>

Soya Formulas-OTC		
	Age Range	Notes
SMA Wysoy (800 gms)	6 months onwards	Lactose free, Contains Omega 3 (DHA), Suitable for vegetarians, vegan diet
Infasoy (Cow and Gate) (900 gms)	6 months onwards	Lactose Free, Halal Approved, suitable for vegetarians, vegan diet
Enfamil Prosobee (Plant based)(624gm)	6 months onwards	Lactose Free, Suitable for Halal and Kosher, suitable for vegetarians, vegan diet

Appendix 2: Other dietary requirements (halal & kosher formulas) ⁽⁵⁾

Milk name	Manufacturer	Halal	Kosher	Vegan
Alfamino®	Nestle	Yes	No	No
Althera	Nestle	Yes	No	No
Aptamil Pepti®	Danone/Nutricia	No	No	No
Elecare	Abbott	Yes	Yes	No
Neocate Syneo®	Nutricia	Yes	Yes	No
Neocate LCP®	Nutricia	Yes	Yes	No
Nutramigen LGG®	Mead Johnson	No	No	No
Puramino®	Mead Johnson	Yes	Yes	No
Similac Alimentum®	Abbott	No	No	No
Wysoy®	SMA	Yes	No	Yes
Infasoy	Cow and Gate	Yes	No	Yes

Note: formulations may be subject to change at the discretion of the manufacturers.

Appendix 3: Improving acceptability of milk free formulas:

EHF and AAF (see second line options) have an unpleasant taste and smell, which is better tolerated by younger patients. Some babies, especially those younger < 12 weeks might have no issues with acceptability. Unless there is IgE mediated or severe allergy, advice parents to introduce the new formula gradually by mixing with the usual formula 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. Paediatric Dieticians will be able to support with specific advice if required.

Lactose-containing products (Althera and Aptamil Pepti) aids the palatability of the formula; however some CMA babies may have temporary lactose intolerance in addition to their milk allergic symptoms.

Appendix 4: Other milk related conditions

1. Cow's milk protein proctocolitis (FPIAP)

Food protein-induced allergic proctocolitis (FPIAP) is a type of delayed inflammatory non-IgE mediated gut food allergy. Symptoms usually start at one to four weeks of age and range from having blood, which is sometimes seen with mucous in bowel movements, to blood stained loose stools or diarrhoea. Infants with FPIAP are usually otherwise healthy and growing well. FPIAP mostly occurs in breastfed infants but can also occur once cow's milk or soy-based formula is commenced. The main triggers are cow's milk or soy. It improves when cows' milk protein is eliminated from the maternal diet. This usually resolves by a year of age when normal cows' milk can be re-introduced. This is a non-IgE-mediated cows' milk protein allergy.

2. FPIES (food protein-induced enterocolitis syndrome)

FPIES is a rare condition which presents in infants with profuse vomiting, diarrhoea, acidosis and shock, 1-3 hours after ingestion of milk or other food proteins.

- The child may be assessed for sepsis.
- It may be associated with a raised white cell count, but the child is afebrile and stool samples are clear.
- FPIES requires hospital referral.
- This is a non-IgE-mediated food allergy.

3. Lactose Intolerance

Lactose intolerance

Symptoms include:	<ul style="list-style-type: none">• Abdominal bloating• Increased wind• Loose green stools) Usually occurs following an infectious GI illness) but can occur alongside new or) undiagnosed coeliac disease)
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Low lactose/lactose free formula	Available to buy over the counter from supermarkets & should be purchased SMA LF®/ Aptamil Lactofree etc, Soya formulas are also Lactofree In children over one year suggest use of lactose free full fat cow's milk, yoghurt and other dairy products which can be purchased from supermarkets (Lactofree® brand)
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Review after 2 weeks to see if symptoms have improved – consider alternative diagnosis if no improvement in symptoms.

Continue low lactose/lactose free formula for a few weeks to allow resolution of symptoms then advise parent to slowly start to re-introduce standard formula/milk into diet.

Refer to secondary or specialist care if symptoms have not resolved on commencement of standard formula/milk.

NOT APPROPRIATE IF INFANT HAS SUSPECTED COW'S MILK ALLERGY

Appendix 5- Gastro-oesophageal reflux

Gastro-oesophageal reflux disease (GORD)	
<p>Gastro- oesophageal reflux (GOR) is the passage of gastric contents into the oesophagus. It is a normal physiological process that usually happens after eating in healthy infants, children, young people and adults. Gastro- oesophageal reflux disease (GORD) occurs when the effects of GOR leads to symptoms severe enough to require medical treatment.</p>	
Symptoms include:	<ul style="list-style-type: none"> • Vomiting (usually in the first 6 months of life) • Regurgitation of significant volumes of feed • Reluctance to feed • Crying at feed times/distress • Faltering Growth • Small volumes of feed being taken • Irritability • Back arching/ choking • Chronic cough
<p>Treatment of GORD</p> <p>In well infants with / without effortless regurgitation of feeds, provide reassurance and monitor. Symptoms resolve in 90%of infants by 1 year of age. Do not investigate/ treat if possets/ regurgitates but no other symptoms of distress. Advice from Health visitor on responsive, paced breast/ bottle feeding</p> <p>In breastfed or formula fed infants with frequent regurgitation and marked distress, take a stepped approach (Refer to NICE guideline: Gastro-oesophageal reflux disease in children and young people: diagnosis and management)</p>	
<p>Rule out overfeeding by establishing the volume and frequency of feeds. Average requirement of formula is 150 mls/kg/day for babies up to 6 months and should be spread over 6-7 feeds.</p>	
Step 1	Give parental reassurance and practical advice on avoidance of over feeding, positioning during and after feeding before moving to step 2.
Step 2	<p>FIRST LINE (for formula-fed infants): 2 week trial (with planned review) of one anti-reflux formula in primary care:</p> <ul style="list-style-type: none"> • Cow and Gate anti-reflux®, Aptamil anti-reflux® or SMA Stay Down® are available over the counter from supermarkets & should be purchased. • Enfamil AR® is available from community pharmacies or on prescription <p>Alternatively, or if trial of anti-reflux formula not successful or not tolerated, Instant Carobel® can be added to the usual milk</p> <p>SECOND LINE (for formula-fed infants): stop the anti-reflux formula and trial of Infant Gaviscon® for 2 weeks (as per dosing recommendations in BNFC).</p> <p>FIRST LINE (for breast-fed infants): trial of Gaviscon® for 2 weeks (as per dosing recommendations in BNFC)</p>
<p>Review after two weeks. If symptoms are not improved despite above efforts, consider pharmacological treatment (H2 Antagonists (Ranitidine currently Not available), Proton Pump inhibitors, sharing risks and benefits of medications with parents or a trial of Cows milk protein exclusion.</p>	

Thickened formula – Available OTC - DO NOT prescribe		
Aptamil® Anti-Reflux (900g) (Milupa)	From birth until 12 months	Contains carob bean gum
Cow and Gate® Anti-Reflux (900g)		Contains carob bean gum
SMA® Anti-Reflux (800g)		Contains corn starch
Notes		
<ul style="list-style-type: none"> • Alternatively, prescribe Carobel to add to regular milk formula and titrate as needed • Do not use thickened formula alongside alginate therapy e.g. Gaviscon or carobel • Parents should refer to manufacturers’ guidance on how to prepare thickened formula. <p>Note: This is currently not in line with DOH guidance on safe preparation of infant formula and parents should be made aware of the risk of infection.</p> <ul style="list-style-type: none"> • If symptoms resolve continue but review and trial infant first milk at intervals. 		

When to consider Non-IgE CMA in those with Reflux?

- Existing atopic disease, in particular eczema in infants
- First degree relative with food allergy or atopic disease
- **More than one** of the following are present: GOR/GORD, chronic loose stools, blood or mucus in stools, abdominal pain, food refusal or aversion, constipation, peri-anal redness, pallor and tiredness, faltering growth in conjunction with one or more gastrointestinal symptoms (with or without atopic eczema) ^(11,12).

Possible CMPA – if present, consider 2- 4 weeks of cows' milk protein exclusion (maternal if breastfed, eHF if formula fed) under dietetic guidance, before a trial of H1 antagonist/ PPI ^(11, 12)

Resources for Parents

- [Cow's Milk Free Diet for Infants and Children; British Dietetic Association 2020.](#)
- [iMAP guideline: The Early Home Reintroduction to Confirm the Diagnosis of Cow's Milk Allergy](#)
- [iMAP Milk Ladder](#)
- [iMAP milk ladder receipes](#)
- [iMAP fact sheet for infants with symptoms of a possible mild to moderate non-IgE mediated allergy whilst being exclusively or partly breastfed](#)
- [Allergy UK Quick guide: Does my child have a Cows Milk allergy ?](#)
- [Allergy UK Quick Guide: Cow's Milk Free Diet Information For Babies and Children](#)
- [Allergy UK leaflet: Could it be Cow's Milk Allergy ?](#)

Resources for Professionals

- [Presentation of Suspected Cow's Milk Allergy \(CMA\) in the 1st Year of Life algorithm](#)
- [iMAP Treatment algorithm: Management of Mild to Moderate Non-IgE Cow's Milk Allergy \(CMA\)](#)

Appendix 7 -Useful online resources:

- British Society for Allergy and Clinical Immunology (BSACI) website. Available at <http://www.bsaci.org/index.htm>
- Allergy UK factsheets. Available at: <https://www.allergyuk.org/information-and-advice/conditions-and-symptoms>.
- National Health Service: What should I do if I think my baby is allergic or intolerant to cows' milk? Available at: <https://www.nhs.uk/common-health-questions/childrens-health/what-should-i-do-if-i-think-my-baby-is-allergic-or-intolerant-to-cows-milk/>.
- iMAP Milk Ladder. Published Oct 2013, available at: <http://ifan.ie/wp-content/uploads/2014/02/Milk-Ladder-2013-MAP.pdf>.
- Allergy UK, Types of food allergy. Available at: <https://www.allergyuk.org/information-and-advice/conditions-and-symptoms/36-types-of-food-allergy>.
- British Dietetic Association, Food factsheets. Available at <https://www.bda.uk.com/foodfacts/home>.

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11. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). *Journal of Pediatric Gastroenterology and Nutrition* 2009; 49: 498-547. <http://www.naspghan.org/files/documents/pdfs/position-papers/FINAL%20-%20JPGN%20GERD%20guideline.pdf>
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