

Managing cows' milk protein allergy in infants

Dietary avoidance of cows' milk is the only management strategy for infants with cows' milk protein allergy (CMPA). If continued breastfeeding is not possible, infants with CMPA should be transitioned to a non-cows' milk infant formula. From 1 July, 2020, Special Authority criteria for accessing amino acid infant formula as a funded milk substitute will change, so primary care will need to begin planning for patients who may be affected.

KEY PRACTICE POINTS:

- Recognising cows' milk protein allergy (CMPA) in primary care is sometimes challenging as infants can present with a diverse range of non-specific symptoms; making the correct diagnosis is important so that infants are not unnecessarily subjected to dietary exclusions
- The only effective treatment for CMPA is dietary avoidance of cows' milk, which may also include avoidance of products containing milk and restriction of cows' milk consumption by the mother if the infant is breastfed
- If continued breastfeeding is not possible for infants aged under 12 months, a non-cows' milk formula should be trialled; options include soy formula (not funded), extensively hydrolysed formula (eHF) or in some cases amino acid formula (AAF)
- Both eHF and AAF are funded with separate Special Authority approval criteria:
 - eHF is generally well-tolerated and should be the first-choice funded formula for most infants with CMPA
 - AAF is used for infants with severe or complicated conditions related to CMPA; it is currently over-prescribed
- The Special Authority criteria for accessing funded AAF will change on 1 July, 2020:
 - eHF must have been trialled first unless the infant has a history of anaphylaxis to cows' milk protein or eosinophilic oesophagitis
 - Applications for infants aged under 12 months can be made by any relevant practitioner, including nurse practitioners and prescribers
 - Applications for children aged over 12 months can only be made by a paediatrician, paediatric gastroenterologist or paediatric immunologist, or by a dietician on the recommendation of one of these specialists
- CMPA often resolves in early childhood; children with CMPA should be regularly re-evaluated as to whether cows' milk can be re-introduced into their diet
 - Children aged over 12 months may no longer require any infant formula as there is reduced requirement for milk as a primary nutrition source after this age

Cows' milk protein allergy (CMPA) in infants

CMPA is an adverse immune response that occurs in approximately 2–3% of children before the age of three years.¹ Sensitivity can occur to more than one type of milk protein, and cross-reactivity with other animal milk proteins such as goats milk is very common.² Infants usually present with CMPA during the first few months of life, and in many cases, management can remain solely within primary care.¹ CMPA is reported to resolve in approximately half children before the age of 12 months, and in up to 90% by the age of five years.³ However, more recent evidence suggests that time to resolution is dependent on the type of CMPA (see: "CMPA is a spectrum of syndromes").⁴

CMPA is a spectrum of syndromes

Immune responses associated with CMPA can be IgE-mediated (immediate) or non-IgE-mediated (delayed), and there is a wide spectrum of possible reactions, ranging from mild gastrointestinal manifestations through to anaphylaxis.* (Table 1):^{1, 5–7}

- **IgE-mediated CMPA** – the onset of symptoms typically occurs within minutes of ingestion but may occur up to two hours later. IgE mediated CMPA often co-exists with allergies to other foods, such as eggs and peanuts. Reactions may involve:
 - **Skin** – with redness, pruritis, urticaria or angioedema
 - **Gastrointestinal tract** – vomiting, diarrhoea or abdominal pain
 - **Respiratory** – coryza, stridor, cough or wheeze
 - **Cardiovascular** – infants may present pale and floppy
- **Non-IgE-mediated CMPA** – symptoms typically occur more than two hours or even days following ingestion. Reactions usually involve the gastrointestinal tract, e.g. vomiting, diarrhoea, blood in the stools, and more rarely may also include the skin and respiratory tract.

* Note: anaphylaxis refers to any IgE-mediated reaction with respiratory or cardiovascular features.

CMPA is generally self-limiting, however, resolution of non-IgE-mediated CMPA is generally more rapid than for the IgE-mediated form.⁴ In a 2015 European study of children with confirmed CMPA diagnosed before the age of two years, 69% tolerated cows' milk when re-challenged after one year.⁸ However, when evaluated based on the type of CMPA diagnosed, 100% of the children with non-IgE-mediated CMPA had recovered, compared with only 57% of those with the IgE-mediated form.⁸

Establishing a diagnosis of CMPA

Making a clear diagnosis of CMPA can be difficult, particularly as many symptoms are non-specific, e.g. reflux, diarrhoea, vomiting, and many overlap with other conditions infants commonly present with in primary care (Table 1).⁷ In some cases, irritability and colic are the only symptoms that are present.⁶ As a result, CMPA is often over-diagnosed or other conditions are mislabelled as CMPA (see: "Differentiating lactose intolerance and non-IgE mediated CMPA"). A prospective cohort study demonstrated that 64% of infants exhibiting a possible adverse reaction to cows' milk were incorrectly suspected of having CMPA before testing was performed that excluded it as a diagnosis.¹² Conversely, delaying or under-diagnosing CMPA can result in unnecessary morbidity, adverse nutritional or behavioural outcomes, and parental anxiety.¹³

Remember that spilling is a normal infant behaviour.

While vomiting is associated with several CMPA syndromes, it should be recognised that "spilling" is a distinct behaviour that is common before age 12 months. Infant spilling can be defined as regurgitation two or more times per day for three or more weeks in otherwise healthy infants aged three weeks to 12 months.¹⁴ The pattern and volume of spilling varies widely between infants, however, it is typically only a portion of the milk feed. Infant spilling is not associated with retching, haematemesis, aspiration, apnoea, failure to thrive, feeding or swallowing difficulties, abnormal posturing or accompanying tissue damage.¹⁴ In contrast, these features may be present with vomiting, which is a central nervous system reflex, involving forceful expulsion through the mouth due to co-ordinated movements involving the small bowel, stomach, oesophagus, and diaphragm. Vomiting as a symptom of CMPA is likely to involve the expulsion of large volumes of milk feed, and invariably be distressing for the infant, and is more likely to be accompanied by other clinical features (rather than occurring in isolation).

Review the infant's allergic clinical history

If an infant is suspected of having CMPA, the first step is to take an allergy-focused clinical history. This process will also inform further investigations (Table 1).

In general, clinicians should aim to identify:¹

- Presenting symptoms and signs that may indicate possible CMPA, including age of onset, timing of onset following ingestion, reaction duration, severity and frequency
- The infant's feeding history, including identifying sources of cows' milk protein in the infant's and mother's diet (if breastfed), the frequency of feeding (if breastfed), the quantity consumed (if bottle-fed), and any concerns regarding difficulty feeding or growth

- Details of any previous management, including medicines and the response to any treatment or dietary change
- Any history of atopic conditions in the infant or a first degree relative, i.e. parents or siblings

Interpreting the findings. The allergy-based clinical history should provide a clear distinction between IgE- and non-IgE-mediated reactions, particularly in terms of the timing, nature of symptoms and family history:¹

- A history of immediate allergic symptoms in response to cows' milk ingestion strongly supports a diagnosis of IgE-mediated CMPA
- Diagnosing non-IgE mediated CMPA is generally more difficult, particularly as the symptoms have a slower onset in relation to ingestion, they can vary significantly and may be localised to the gastrointestinal tract

CMPA is less prevalent in infants that are exclusively breastfed (0.5%) compared with the overall population (2–3%) as their only exposure to cows' milk protein comes through the maternal diet, which is associated with a low risk of clinical allergy.¹³ Therefore, it is important to not over-interpret minor symptoms in exclusively breast-fed children. Any family history of atopic conditions, however, makes a diagnosis of CMPA more likely.¹

For suspected non-IgE-mediated CMPA reactions:

A trial elimination of cows' milk in the infants diet for two to four weeks is suitable in most infants with mild-to-moderate non IgE-mediated CMPA symptoms and signs.^{1, 13} This should encompass all possible sources of cows' milk, including dairy products such as yoghurt and cheese. Breastfeeding should continue to be actively supported, with maternal avoidance of cows' milk.¹³ If infants cannot continue exclusive breastfeeding,

or they are already formula feeding, they will require a non-cows' milk formula during this time (see: "Management of CMPA in infants"). For infants with suspected severe non-IgE reactions, consumption of cows' milk should stop, and they should be urgently referred to secondary care.

If the infant's symptoms clearly improve during an elimination trial of two to four weeks: re-introduce cows' milk to observe whether symptoms return, thereby confirming CMPA; this can be done at home.¹ However, if there is still uncertainty, then more specific testing may be required (Table 1). Allergy testing (e.g. skin prick) is generally not necessary.

If the infant's condition does not improve following an elimination trial of two to four weeks: consider other possible sources of cows' milk, e.g. baked goods. However, tolerance to milk in processed products does not exclude CMPA as production methods such as heating and fermentation can diminish the amount of allergen present. In addition, alternative diagnoses should be investigated, and the infant may need to be referred to a paediatrician or allergy specialist.

For suspected IgE-mediated CMPA reactions:

For infants suspected of having an IgE-mediated CMPA reaction based on their allergic history, e.g. immediate urticaria following cows' milk consumption, a challenge with cows' milk is not generally recommended in primary care.⁶ Cows' milk should be immediately excluded from the infant's diet and they should undergo allergy testing, e.g. serum allergen-specific IgE or skin prick testing, and referral to a paediatrician or allergy specialist should be considered.¹³ This history alongside a positive allergy test is sufficient to confirm a diagnosis of IgE-mediated CMPA. In all cases of anaphylaxis, the infant should be urgently referred to secondary care for management without the need for initial allergy testing.

Lactose intolerance can be differentiated from non-IgE mediated CMPA with an elimination trial

Non-IgE mediated CMPA is often confused with lactose intolerance; although they can co-exist.⁷ This is problematic as mislabelling lactose intolerance as CMPA may result in unnecessary dietary restriction when a low-lactose diet would suffice. The key distinction between the two conditions is that CMPA is an immune-mediated reaction, while lactose intolerance involves a reduced capacity to digest lactose (a disaccharide). Lactose intolerance only causes symptoms in the bowel, e.g. diarrhoea, abdominal pain, bloating, and is not generally associated with rectal

bleeding. Conversely, non-IgE mediated CMPA symptoms can be gastrointestinal, skin or rarely respiratory (as seen in Heiner's syndrome), and reactions such as proctocolitis can cause rectal bleeding.⁷

Both conditions can be investigated by trialling dietary exclusion of cows' milk. Symptoms are likely to improve within 48 hours of exclusion for infants with lactose intolerance, while non-IgE mediated CMPA symptoms often take at least two weeks to improve (sometimes longer).^{5, 7}

Table 1. Clinical presentations and differential diagnosis of IgE-mediated and non-IgE-mediated CMPA.^{4,8-11}

Immune type	Condition	Time to reaction following ingestion	Clinical features	Distinguishing features	Occurrence in exclusively breastfed infants	Differential diagnosis	Potentially useful investigations (some of which are performed in secondary care)
IgE	Acute allergic reaction (non-anaphylactic)	Immediate, up to two hours	Perioral or orbital angioedema/erythema, generalised urticaria, vomiting, diarrhoea	No recurrence if cows' milk is completely avoided. Incidence approximately 2% in infants	Possible	Idiopathic/viral induced urticaria	Skin prick test, IgE antibodies. [†] An oral inpatient challenge may be considered but is not required for a diagnosis if there is a clear correlation between consumption of milk and the onset of symptoms.
	Anaphylaxis	Immediate, up to two hours	Respiratory +/- cardiovascular involvement often associated with above features	As above. IM adrenaline preferably in the midpoint of the anterolateral thigh is the treatment of choice. Rare manifestation of CMPA	Extremely rare	Sepsis, acute cardiovascular or respiratory compromise, seizures	Skin prick test, IgE antibodies. [†] An inpatient challenge is not indicated.
Mixed (IgE and non-IgE)	Atopic dermatitis (eczema)*	Highly variable: min/ hours/days	Pruritic rash	Infants: cheeks, trunk, extensor surfaces Older children: flexure surfaces, face, eyelids Approximately 70% of cases occur in infants aged 3–6 months, however, the incidence due to CMPA unknown	✓	A wide variety including seborrhoeic dermatitis, psoriasis, acrodermatitis enteropathica	Cows' milk elimination and re-challenge
Non-IgE	Eosinophilic oesophagitis**	Days	Vomiting, irritability, feed refusal, failure to thrive, oesophageal dysmotility	Histological diagnosis, unresponsive to proton pump inhibitors. Extremely rare with variable age of onset (less likely in older children). A family history is common	Extremely rare (case reports)	GORD, mucosal candidiasis, Crohn's disease	Endoscopy, eosinophil count
	Food protein-induced enterocolitis syndrome (FPIES)	Vomiting 2–4 hours Diarrhoea 5–10 hours	Profuse vomiting +/- diarrhoea, sudden onset of pallor and floppiness. Around 20% present as hypovolaemic shock (with associated metabolic acidosis and methaemoglobinaemia)	Responds to fluid resuscitation, adrenaline not required. Half of affected children outgrow the condition by three years of age	Extremely rare (case reports)	Sepsis, gastroenteritis, malrotation, intussusception, metabolic disorder	Clinical diagnosis with a focus on history, no laboratory markers available (a raised white blood cell count often adds to clinical confusion)
	Cows' milk protein-induced GORD	Hours/days	Frequent regurgitation, poor feeding, feed aversion, failure to thrive, symptoms indicative of tissue damage e.g. haematemesis	Partially responsive to proton pump inhibitors when underlying mechanism related to CMPA. Up to 40% of infants with GORD have CMPA	✓	Idiopathic GORD, eosinophilic oesophagitis, malrotation	Clinical diagnosis. Requires endoscopy if haematemesis or significant failure to thrive
	Enteropathy	Hours/days	Vomiting, diarrhoea, severe irritability, failure to thrive, iron deficiency anaemia, protein losing enteropathy	Receiving cows' milk in diet. Unknown incidence due to CMPA	✓	Lactose intolerance, coeliac disease giardiasis, immune deficiencies, autoimmune enteropathy	Small bowel biopsy for histology, duodenal disaccharidases and microscopy of duodenal aspirate for giardia
	Proctocolitis	Hours/days	Low-grade rectal bleeding and mucus in stool in an otherwise well infant usually within the first three months of life	Normal perianal inspection, thriving. CMPA is the most common cause	✓	Necrotising enterocolitis, constipation with anal fissure, infantile inflammatory bowel disease, chronic granulomatous disease, juvenile polyp	Rectal biopsy only if atypical features or non-responsive to treatment (eosinophils predominate). If symptoms are prolonged monitor haemoglobin and ferritin levels.
	Heiner's Syndrome (milk-induced pulmonary disease/haemosiderosis)	Hours/days	Cough, wheezing, recurrent fever, nasal congestion, recurrent otitis media, failure to thrive, haemoptysis, dyspnoea, colic, anorexia, vomiting and diarrhoea, blood in stool	Extremely rare. Patients may have IgG antibodies to cows' milk protein (and in some cases IgE antibodies will be present). Peripheral eosinophilia is often seen. Responds to dietary elimination	Unknown	Idiopathic pulmonary haemosiderosis, chronic bronchopneumonia, aspiration pneumonia	Chest X-ray (looking for pulmonary infiltrates), cows' milk elimination and re-challenge
Potentially Non-IgE – unlikely to be isolated or a sole manifestation	Colic	Hours/days	Paroxysms of unexplained, inconsolable crying (more than 3 hours a day, more than 3 days per week for at least 3 weeks)	Responds to dietary elimination, more likely if it presents soon after the introduction of cows' milk protein in the diet	✓	Idiopathic colic, developmental disorders, urinary tract infection	Cows' milk elimination and re-challenge
	Constipation	Hours/days	Passage of infrequent and/or hard stools	Responds to dietary elimination, more likely if it presents soon after the introduction of cows' milk protein in the diet	✓	Hirschsprung's disease, slow transit constipation	Cows' milk elimination and re-challenge in conjunction with laxative treatment. Consider rectal biopsy in infants with early-onset severe constipation

* Atopic dermatitis as a sole manifestation of CMPA is debated in the literature, and it is important to establish whether other stimuli are potential triggers, such as laundry powder or soap.

** There is a lack of expert consensus as to whether eosinophilic oesophagitis is a primary non-IgE-mediated reaction, or a mixed immune reaction. However, most guidelines define it as non-IgE-mediated.

† Higher IgE levels are predictive of a longer duration of CMPA.

CMPA, cows' milk protein allergy; GORD, Gastro-oesophageal reflux disease; IM, intramuscular.

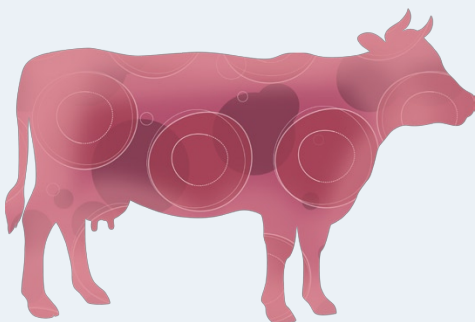
Recommendations for referral to secondary care

Infants with severe or resistant symptoms and signs of CMPA should be referred to secondary or emergency care with the urgency of referral depending on their specific clinical scenario. This includes:^{1, 9, 13}

- Anaphylaxis
- Severe failure to thrive
- Any severe, persisting or treatment-resistant gastrointestinal or skin symptoms, e.g. persistent rectal bleeding and/or vomiting, severe atopic dermatitis
- Hypoproteinaemia/protein losing enteropathy (clinical features include vomiting, diarrhoea, severe irritability, failure to thrive, iron deficiency anaemia)
- Food protein induced proctocolitis (low grade rectal bleeding in otherwise healthy infants)

Dispelling dietary myths: cows' milk does not increase the risk of type 1 diabetes

It has historically been thought that avoiding cows' milk protein in favour of elemental infant formulas (such as eHF or AAF) reduces the infant's risk of developing type 1 diabetes, as previous research suggested this may potentially be the case. However, recent studies suggest there is no increase in pancreatic islet autoimmunity through the avoidance of cows' milk.^{15, 16} In fact, there may even be an increased risk of type 1 diabetes in children receiving eHF compared with non-hydrolysed cows' milk formulas as a first choice.^{15, 16} Clinicians should therefore emphasise that the decision to avoid cows' milk protein should be made based on medical indication of CMPA rather than parental preference.



Managing CMPA in infants following diagnosis

1. Exclude cows' milk

Avoidance of cows' milk is the only treatment for CMPA.⁵ Regardless of the underlying cause and clinical type of CMPA, any dietary consumption of cows' milk should be eliminated following diagnosis; this includes both direct sources in the infant's diet (e.g. cows' milk, cows' milk formula or solid foods containing cows' milk) and potentially maternal cows' milk consumption if the infant is breastfed (see: "Breast is best, until it's not"). For infants with mild-to-moderate CMPA symptoms, solid foods containing milk may potentially still be able to be consumed because in some cases the production process significantly diminishes the amount of allergen present.

A nutritional assessment should ideally be performed in primary care following any decision to remove cows' milk protein from an infant's diet (or the mother's) to ensure the amounts of protein, calories and micronutrients (e.g. calcium and vitamin D) are adequate. However, calcium supplementation is usually not required.⁵ Other dietary sources of calcium should be encouraged provided they are age appropriate and the infant does not have a proven allergy to them, e.g. some breakfast cereals, tofu, dark leafy vegetables.

2. "Breast is best, until it's not"

Exclusive breast feeding is recommended in infants until age six months, at which point it is not sufficient alone for growth and development.¹⁷ Infants generally should continue to be breastfed until they are aged at least 12 months, however, solids should be progressively introduced from around the age of six months (not before four months).¹⁷

Infants with CMPA should continue breast feeding if possible.^{1, 13}

- **Exclusively breastfed infants** – eliminate cows' milk protein from maternal diet
- **Mixed feeding infants** – eliminate cows' milk protein from the infant's diet first; the mother may be able to continue consumption of milk in some cases of delayed reactions; if there are residual symptoms, or if the infant has an immediate CMPA reaction, maternal cows' milk protein exclusion is recommended

If maternal exclusion of cows' milk does not resolve symptoms, or if breastfeeding is problematic or not solely adequate, or if the mother wishes to wean the infant before they are aged 12 months, then infant formula will be required.

3. Selecting an appropriate infant formula

Only three types of formula are recommended for infants with CMPA: **(1)** soy formula (not funded), **(2)** extensively hydrolysed formula (eHF) and **(3)** amino acid formula (AAF).¹⁸ Both eHF and AAF are fully funded with Special Authority approval (separate application criteria). Other formulas such as goats'-milk based, lactose-free and partially hydrolysed formula are not suitable for infants with CMPA due to the potential for cross-reactivity against proteins with a similar structure, or direct immune responses against conserved proteins. Alternative "milk beverages", such as rice or almond milk, are nutritionally inadequate and therefore not recommended as a substitute for breast or cows' milk.⁵

Extensively hydrolysed formula (eHF) is the first-line choice formula for most infants with CMPA

The age of the infant and the clinical characteristics of the CMPA should determine the type of formula most appropriate as an initial option. However, in the majority of cases, eHF is recommended as the first-line choice of infant formula

for CMPA (Table 2).^{1, 13} Hydrolysis of cows' milk breaks down potentially allergenic proteins into less-reactive peptides, making an immune response less likely. As a result, CMPA symptoms resolve in approximately 90% of infants that transition to eHF.⁵

Soy can be discussed as an alternative to eHF in infants aged over six months

Soy-based formula is not funded in New Zealand but is comparable in price to standard cows' milk formula. In some cases, infants may find soy formula more tolerable than eHF and therefore its use can be discussed as a possible alternative, e.g. non-anaphylactic CMPA associated with gastrointestinal symptoms (Table 2).⁶ However, soy formula is not considered to be suitable for children aged under six months as rates of concurrent soy allergy are higher in this group.¹⁹

Amino acid formula (AAF) should be reserved for complicated or severe conditions

AAF is considered to be the closest formula option to being "non-allergenic" as it consists of individual amino acids.²⁰

Table 2: Appropriate choice of formula feed in infants with CMPA syndromes in primary care.^{1,6}

Syndrome	First choice	Second choice (if first not tolerated)
IgE		
Acute allergic reaction (non-anaphylactic)	eHF or soy* (if aged >6 months)	eHF (if soy was trialled first) or AAF [†]
Anaphylaxis	AAF (with urgent referral)	–
Mixed immune response (IgE- and non-IgE)		
Atopic dermatitis (eczema)	eHF or soy* (if aged >6 months)	eHF (if soy was trialled first) or AAF [†]
Non-IgE		
Eosinophilic oesophagitis	AAF	–
Food protein-induced enterocolitis syndrome	eHF	AAF
Food protein-induced proctocolitis	eHF	AAF
Gastrointestinal syndromes, GORD, allergic eosinophilic gastroenteritis, food protein-induced enteropathy, constipation, severe irritability (colic)	eHF or soy* (if aged >6 months)	eHF (if soy was trialled first) or AAF [†]

* Soy formula is not funded but may be used as an alternative to eHF for some infants with mild CMPA symptoms.

† eHF must first be trialled first for 2–4 weeks and found to be inappropriate due to severe intolerance, allergy or malabsorption.

AAF, amino acid formula; eHF, extensively hydrolysed formula; GORD, gastro-oesophageal reflux disease

Despite being highly tolerable, its current use as a funded formula is controversial as it is approximately three times more expensive to produce than eHF, and eHF will be sufficiently hypoallergenic in most infants.^{21,22} Therefore, access to funded AAF should not be based on a preference; there needs to be a medical requirement for it (Table 2).

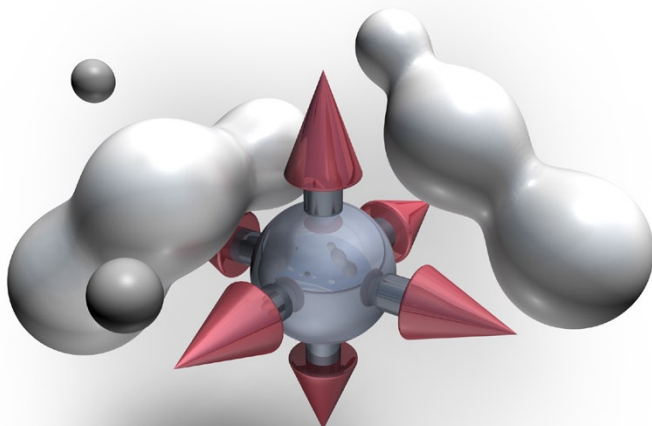
The indications for AAF in infants with CMPA include:²⁰

- Anaphylaxis
- Eosinophilic esophagitis
- Severe intolerance, allergy or malabsorption on eHF
- Growth faltering, particularly with multisystem involvement and multiple food exclusions

Currently, many infants are inappropriately prescribed AAF. In children aged 12 months or older, the expected prescribing ratio for eHF to AAF should be approximately 3:1, however, under the current subsidy criteria it is estimated to be an almost 1:1 ratio.²² Most children have a reduced requirement for milk once they are aged over 12 months and should be able to progress to solids as their primary source of nutrition, meaning that dependence on AAF can be avoided or reduced. However, the timing of this dietary transition will differ between children, and there are no clear recommendations for weaning off formula. It may be appropriate to consult with a paediatrician or dietitian with expertise in the management of CMPA for further advice.

4. Long-term re-introduction of cows' milk

In most cases, CMPA is a self-limiting condition; resolving between the ages of one to three years in many children.⁴ Therefore, in the long-term it is important to regularly review and consider a cows' milk challenge to avoid unnecessary dietary restriction.^{1,13} This is required for AAF Special Authority subsidy renewals. Reassessment for tolerance should be on a case-by-case basis, but in general a review every six months is reasonable.^{1,13} However, for some infants with more severe IgE-mediated CMPA this recommendation will not be suitable, and it is best to discuss a tailored re-introduction strategy with their paediatrician.



Changes to Special Authority restrictions on AAF

The current AAF Special Authority criteria

Under the current Special Authority criteria for AAF – which will remain in effect until 30th June, 2020 – an initial application for AAF can be made by any dietitian, relevant specialist or vocationally registered general practitioner if the patient meets one of the following prerequisites:²¹

- eHF has been reasonably trialled (two to four weeks) and is found to be inappropriate due to documented severe intolerance or allergy or malabsorption; or
- History of anaphylaxis to cows' milk protein formula or dairy products; or
- Eosinophilic oesophagitis

Approvals are valid for six months, at which point an assessment of whether the infant can be transitioned to cows' milk, soy or eHF must take place.²¹ If the outcome is that AAF continues to be required, then an application can be made for renewal by any of the listed healthcare professionals above, or by any general practitioner on their recommendation.²¹

What changes are coming?

From 1 July, 2020, the existing Special Authority approval will be replaced with a new form that includes two different sets of funding criteria based on the patients age (Figure 1):²¹

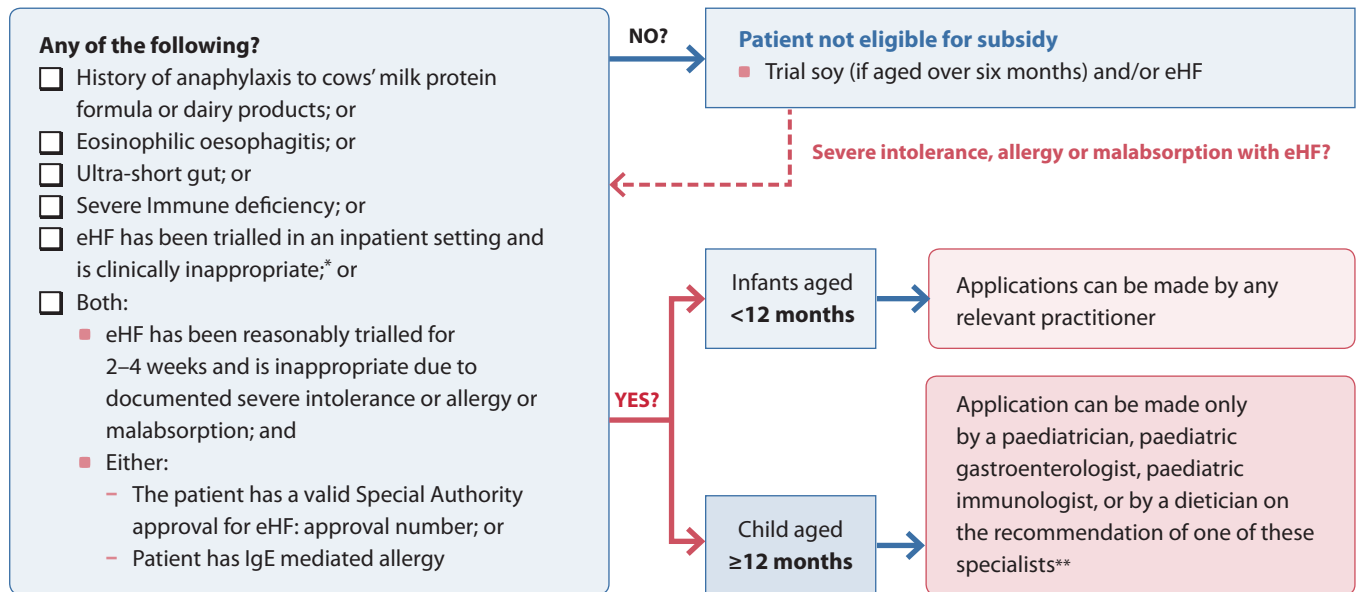
- **Infants up to 12 months of age** – applications can be made by any relevant practitioner (including dietitians, paediatricians, paediatric gastroenterologists, paediatric immunologists, general practitioners, nurse practitioners or nurse prescribers)
- **Children 12 months of age and older** – applications need to be made by a paediatrician, paediatric gastroenterologist or paediatric immunologist, or by a dietitian on the recommendation of one of these specialists

In addition, new criteria will be applied to both age groups (Figure 1):²¹

- Access criteria will now include children with ultra-short gut and severe immune deficiency
- Access criteria will require the following information:
 - Whether the child's cows' milk protein allergy/ intolerance is IgE mediated or non-IgE mediated;
 - That AAF is required for a nutritional deficiency;
 - That there has been a period of three months since the previous application for AAF; and
 - In cases where eHF has previously been trialled:
 - A valid Special Authority number for eHF; or
 - The trial has occurred in an inpatient setting

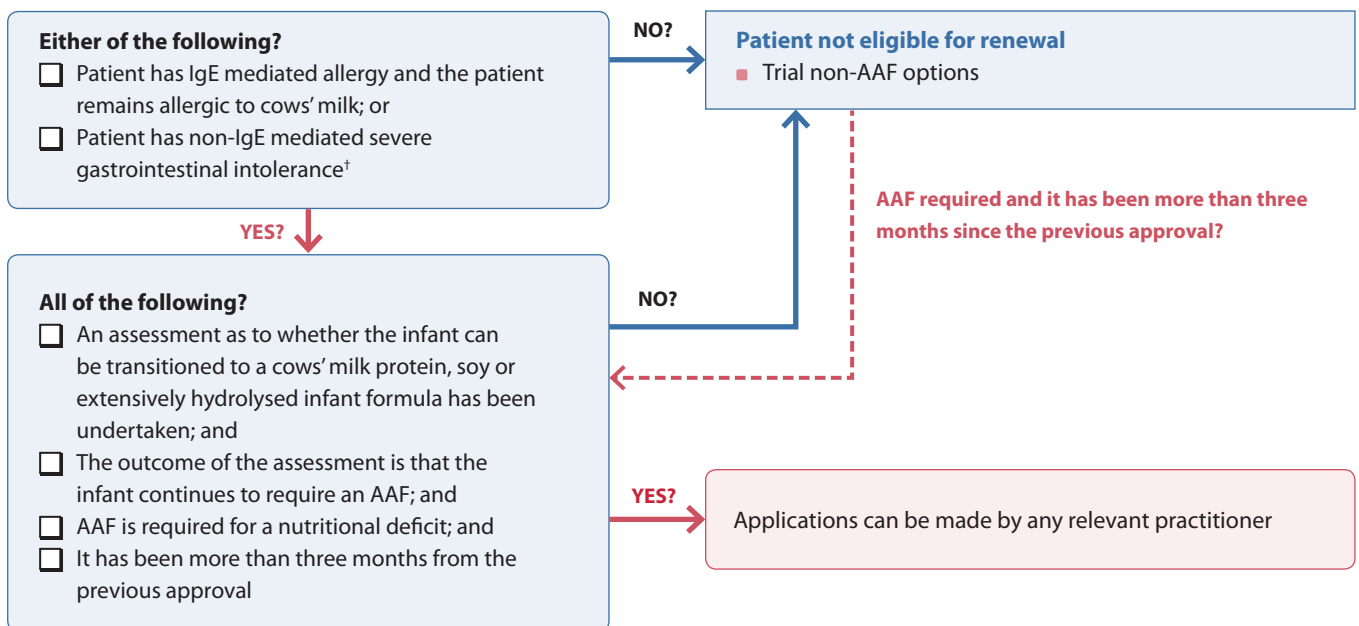
Initial application

(Approvals valid for six months)



Renewal for infants aged <12 months

(Approvals valid for six months)



Renewal for children aged ≥12 months

(Approvals valid for six months)



* This criteria likely applies to children with non-anaphylactic IgE mediated CMPA, where a single inpatient trial of 20 mL of eHF is suitable to establish the need for AAF.

† Including eosinophilic oesophagitis, ultra-short gut and severe immune deficiency.

** Dieticians must have consulted with a paediatrician, paediatric gastroenterologist or paediatric immunologist within the last 12 months.
 AAF, amino acid formula; CMPA, cows' milk protein allergy; eHF, extensively hydrolysed formula.

Figure 1. Special Authority criteria effective from 1 July, 2020 for funded amino acid formula (AAF) in children with CMPA who require formula.²¹

How will Special Authority criteria changes affect the management of patients with CMPA?

These changes allow any relevant prescriber, to make AAF funding applications in primary care for infants aged under 12 months. However, the new criteria also mean that general practitioners and other primary care prescribers will no longer be able to apply for a child's AAF funding renewal once they are aged 12 months or older. Therefore, primary care should begin planning for children likely to still be using AAF on 1 July, 2020 and who will be aged 12 months or older at this date, as they will need to be referred to a dietician, paediatrician, paediatric gastroenterologist or paediatric immunologist. Changes will not be implemented until 1 July, 2020, so this should provide sufficient time to investigate the infant's tolerability to non-AAF formulas or cows' milk, consider a transition from formula to solids as their primary source of nutrition, or schedule secondary care appointments. For AAF subsidy renewals, the patient's IgE status will also need to be established based on the presenting symptoms, i.e. whether they have IgE-mediated or non-IgE-mediated CMPA.

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