NHS Grampian

Guidance For Health Care Professionals On Prescribing Specialist Formulae To Treat Cow's Milk Protein Allergy In Infants And Children

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Policy Statement:

It is the responsibility of all staff to ensure that they are working to the most up to date and relevant guideline, policies, protocols and procedures.

Version 4

Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature: _____

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Revision History:

Revision Date	Previous Revision Date	Summary of Changes	Changes Marked
April 2025	April 2023	Removal of Day 1>1yr old use cows milk.	Page 7, section 2.1
February 2025	April 2023	Updated guidance links throughout document .	Throughout document
February 2025	April 2023	Expanded guidance on calcium vitamin supplement.	Page 6
February 2025	April 2023	Addition of NHS Grampian PPI guidance.	Page 13, section 3.4
February 2025	April 2023	Addition to consultation list.	Page 14, section 7
October 2024	April 2023	Addition of statement supporting breastfeeding.	Page 3, section 1
October 2024	April 2023	Removal of specific branded infant formula.	Page 7, section 2.1
October 2024	April 2023	Added specific details on recommendations on vitamin D and calcium supplementation.	Page 10, section 3.1
October 2024	April 2023	Removal of specific branded infant formula.	Page 10, section 3.1
October 2024	April 2023	Removal of specific branded infant formula.	Page 11, section 3.2
October 2024	April 2023	Removal of specific branded infant formula.	Page 12, section 3.3
October 2024	April 2023	Removal of specific branded infant formula.	Page 13, section 3.4
October 2024	April 2023	Addition of explanation of thickened formula.	Page 13, section 3.4
October 2024	April 2023	Change to first line formula choice – both ENF and AA.	Page 6 – algorithm
October 2024	April 2023	Addition of ‘children with CMPA’ to provide clarity on % given.	Page 5 – section 2
October 2024	April 2023	Statement around preparation of formula milks.	Page 5 – section 2

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1. Introduction

Cow's Milk Protein Allergy (CMPA) currently affects 2 to 4% of all infants in the UK. Most infants will present early - within the first weeks or months of ingesting Cow's Milk Protein (CMP).

Treatment involves complete exclusion of cow's milk protein from the child's diet. If the child is breast fed, the mother should exclude cow's milk. For non-breast fed children, a cow's milk free formula should be used. If the child is on mixed feeding, i.e. breast and bottle fed, a cow's milk free formula should be used. If symptoms only occur on introduction of top up feeds with formula then the mother does **not** need to exclude milk from her own diet. The amount of beta lactoglobulin that is present in breast milk is very small so often infants only present with symptoms when formula is introduced or when introducing solids containing milk proteins.

In all circumstances there should be support given for breast feeding for infants with CMPA and there is no reason to stop but should parents choose to formula feed the following guidance advises on the most clinically appropriate product. A number of different specialist formulae are available on prescription. They are not identical and choice of product is dependent upon clinical symptoms and diagnosis. Review of prescribing data indicates that spend on the products is increasing and there is local and national evidence of inappropriate prescribing of these products.

The aim of this guidance document is to ensure that those health care professionals who are responsible for recognising and treating CMPA are following current international guidelines, are fully aware of the clinical indications for the use of specialist formula and select the most appropriate formula for the individual.

1.1. Definitions and Diagnosis

Cow's Milk Protein Allergy (CMPA) is an allergy to the protein in cow's milk. It is not an intolerance to lactose (milk sugar). It can be:

- IgE- mediated, in which case acute signs or symptoms mostly occur within minutes of ingestion of CMP. Symptoms include immediate reaction with severe respiratory and/or cardiovascular signs and symptoms (rarely a severe gastrointestinal presentation). Skin symptoms tend to be acute urticaria or angioedema.
- Non-IgE-mediated where symptoms run a more chronic course.

Symptoms include:

Gastrointestinal

- Irritability -'Colic' and one or more of the symptoms listed or food allergy in a 1st degree relative.
- Vomiting - 'Reflux' – Gastro-oesophageal Reflux Disease (GORD) unresponsive to thickened feeds and acid suppressive treatment.
- Food refusal or aversion.
- Diarrhoea-like stools loose and/or more frequent.
- Constipation especially soft stools with excessive straining.
- Abdominal discomfort, painful flatus.
- Blood and/or mucus in stools in an otherwise well infant.
- Faltering growth **plus** one or more GI symptoms.

Skin

- Pruritus (itching), Erythema (flushing).
- Non-specific rashes.
- Moderate persistent atopic dermatitis.

Usually several of these symptoms will be present.

Note: Non-IgE-mediated CMPA can, in rarer cases, also be severe. Symptoms can occur 2 to 72 hours after ingestion of CMP and usually include one or more of severe and persisting **gastrointestinal symptoms -** diarrhoea, vomiting, abdominal pain, food refusal or food aversion, significant blood and/or mucus in stools, irregular or uncomfortable stools +/- faltering growth or **skin symptoms** - severe atopic dermatitis +/-faltering growth.

Further information can be found at www.allergyuk.org.

An allergy-focused history is crucial in helping determine between IgE-mediated and non-IgE-mediated reactions. Questions should focus on;

- Any family history of atopic disease in parents or siblings.
- Any history of early atopic disease in the infant.
- The infants feeding history including growth.
- Presenting symptoms and signs that may be indicating possible CMA.
- Details of previous management, including any medication and the perceived response to any treatment or dietary change.

2. Treatment

This guidance document is based on recent UK and European guidelines.[1,2,3,4]

All infants and children should be commenced on a strict cow's milk free diet immediately. Where IgE mediated or severe Non-IgE-mediated CMPA is suspected a referral should also be made to the allergy service within Royal Aberdeen Children's Hospital – health care professionals can email the allergy nurses generic email: gram.paedsallergy@nhs.scot for the Allergy service referral form or for a general query.

The following guidance on management of CMPA refers to those **with mild-moderate non-IgE mediated CMPA.**

If the clinical history suggests non-IgE-mediated CMPA and the child 'has not had a severe delayed reaction', it is recommended to offer a **trial elimination** of cow's milk protein. Issue the leaflet Cows Milk Protein Allergy PIL.pdf

The algorithm on pages 6 and 7 provides full guidance on undertaking the initial trial to confirm diagnosis and the later re-introduction of cow's milk for those where diagnosis has been confirmed.

The clinician is looking for a **clear improvement** in symptoms. The diet should be trialled for 4 weeks (a minimum of 2). It is crucial that milk is re-introduced after the trial period in order to confirm diagnosis. It is important not to skip this step as this can lead to the child remaining on a restricted diet for an unnecessary period of time and can delay diagnosis of an alternative underlying cause of the symptoms.

If the child has not had a **clear** improvement on a cow's milk free diet after the appropriate trial, cow's milk should be introduced into the diet again (either via breast milk with mother back on cow's milk or a suitable formula for non-breast fed children). **There is no need to do this gradually.**

(For those with severe reactions, should they still need an early food challenge to confirm or exclude the diagnosis, this will need to be done under the careful supervision of a specialist allergy team).

Prescribing Specialist Formulae for formula fed/mixed fed infants

Specialist formulae are those products specifically designed to treat CMPA. They can be Extensively Hydrolysed Formula (EHF) or Amino Acid Formula (AAF).

The constituents differ in different formula, however 90% of infants and children will respond to an EHF, therefore these are the first line product of choice. If symptom improvement is uncertain or if symptoms improve then relapse, an AAF should be trialled. It is important that infant milks are made up safely. Powdered infant formula is not sterile and needs to be made up a temperature which will kill any potential bacteria present. All equipment needs to be sterilised.

The treatment algorithm on page 6 provides further guidance. Only a small proportion (10%) of children with CMPA should require an AAF.

Mild-Moderate Non-IgE Cow's Milk Protein Allergy (CMPA) suspected?

Up to 4 week trial- (with a **minimum** of 2 week) of strict milk free diet

Exclusively breast fed?
Strict trial of exclusion of cow's milk from maternal diet
Maternal daily vitamin D and calcium supplement**
Issue leaflet - Cows Milk Protein Allergy PIL.pdf

No indication for use of lactose free milk, goat's milk
No soya milk under 6 months of age

Formula fed/mixed feeding?
Strict trial of Extensively Hydrolysed Formula (EHF)
First line product- SMA Althera
Second line product- Aptamil Pepti 1
No need to exclude milk from the mother's diet

Improvement uncertain

If allergic reaction still suspected
Consider other maternal foods, e.g. egg, soya
Refer to dietitian if necessary

No clear improvement -
CMPA – no longer suspected
Discontinue CMP free diet –see page 6 for guidance
Look for other causes of symptoms

Clear Improvement- Need to confirm diagnosis

Mother to revert to normal diet containing cow's milk foods over 1 week

Use cow's milk formula – See 2.1, page 7 for guidance

Return of symptoms
Exclude cow's milk from maternal diet again
Clear improvement - **CMPA**

No return of symptoms- Not CMPA
Resume normal feeding

Return of symptoms
Resume EHF again
Clear improvement-**CMPA confirmed**

Improvement uncertain- CMPA – still suspected
Consider a 2 to 4 week trial of Mead Johnston- Puramino- Amino Acid Formula (AFF)

No clear improvement-
CMPA – no longer suspected
Discontinue CMP free diet – no need to do this gradually
Look for other causes of symptoms

Continue milk free diet until 9 to 12 months of age or **at least 6 months continued improvement** on a milk free diet*
Issue leaflet - Cows Milk Protein Allergy - Milk Free Weaning PIL.pdf
Calcium+/- Vitamin D** supplement for the mother of breast fed child[3]

A planned re-introduction is then needed to determine if tolerance has been acquired

**All breastfeeding mothers should be taking an over the counter Vitamin D supplement of 10ug. In addition an over the counter calcium supplement will be required along with 3 non-dairy calcium portions to provide a total of 1250mg.

*Consult dietitian for milk free weaning advice if experiencing problems

2.1. Re-Introducing Milk After the Initial 2 to 4 Week Trial Following Clear Improvement in Symptoms

Breast fed

Complete reintroduction of cow's milk or milk containing products for 1 week. These can be fully introduced on day 1 and symptoms monitored over 1 week period – see flow chart on page 6.

Formula fed

Reintroduction of cow's milk formula gradually over 1 week. See table below for reintroduction example.

The Northern Ireland Region Infant Feeding Guidelines recommend[1];

Day 1	30mL of standard first stage cow's milk formula into **one** morning bottle of cow's milk free formula.
Days 2 to 6	Continue to increase the cow's milk formula and reduce the cow's milk free formula using the following example.

Days	Volume of boiled water (mL)	Cow's milk free formula No. of Scoops	Cow's milk formula No. of Scoops
Day 1	180	5	1
Day 2	180	4	2
Day 3	180	3	3
Day 4	180	2	4
Day 5	180	1	5
Day 6	180	0	6

2.2. Home Introduction of Milk at 1 Year or After 6 Months Exclusion for Infants and Children with Mild-Moderate Non-IgE-Mediated CMPA (Milk Challenge)

By 1 year of age around 50% of **infants and children** may achieve tolerance to cow's milk protein and can return to a normal diet[2]. This can be a gradual process with some infants and children only achieving partial tolerance of milk that has been cooked.

In general consider introducing milk around 1 year of age **or after 6 months on a milk exclusion diet.** It is advised that milk protein is gradually reintroduced into the diet as per the iMAP milk ladder.

Infants and children with current atopic dermatitis or **any** history at **any** time of immediate onset symptoms such as pruritus, erythema, acute urticaria (localised or generalised), acute angioedema, cough, chest tightness, wheezing or shortness of breath, should be **challenged in a hospital day case setting**.

Infants and children where milk has caused symptoms such as eczema, urticaria, vomiting, diarrhoea and poor weight gain may be **safely challenged at home**.

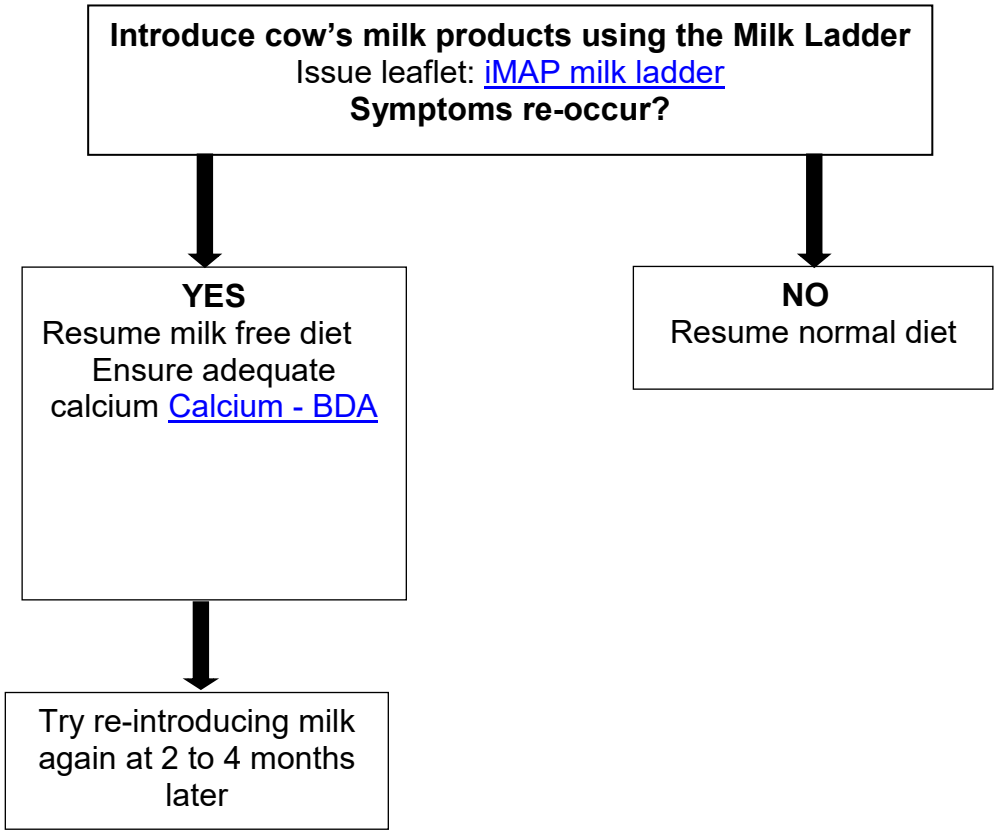
General points

- **Do not** introduce milk if the infant is unwell; if airways are compromised or if eczema is flared up.
- **Do not** introduce milk if the infant is receiving medication that may adversely affect the gut, e.g. a course of antibiotics.
- **Do not** introduce any other new foods when introducing milk.
- Ask the parents to keep a record of the infant's oral intake, stool pattern and symptoms during the milk introduction. For example, re-occurrence of eczema, diarrhoea, increased stool frequency, vomiting.
- There may be a delayed reaction to the introduction of cow's milk therefore infants must be monitored for symptoms for at least 48 hours.
- Advise parents to choose a time during the week, when they can observe the child for a few hours. Note down any reactions, which may be different from the original symptoms.
- If at any time the child is reacting stop the process. The health care professional involved should continue with whatever was previously tolerated and discuss the next steps with a dietitian.

Re-introducing milk

- Give each dose all at once; don't spread it out over the day.
- Allow 4 to 7days on each step before moving onto the next step.
- If the child reacts at any stage continue with what was previously tolerated and discuss with a dietitian.
- Each tolerated food can now be included in the diet.

2.3. Supporting Material



3. Supporting Notes

3.1. Cow's Milk Protein Allergy (CMPA)

Notes[1,2]	Treatment	Prescribing Notes
It is an allergy to the protein in cow's milk **not** the lactose (which is a sugar). Currently affects 2 to 4% of all infants in the UK. Most of these infants will present early - within days or the first few weeks of ingesting Cow's Milk Protein (CMP). It can be: **IgE-antibody-mediated,** in which case acute signs or symptoms mostly occur within minutes of ingestion of CMP. This should be managed in Acute Care. **Non-IgE-antibody-mediated** (previously often referred to as Cow's Milk Protein Intolerance) where symptoms run a more chronic course. Delayed signs or symptoms mostly occur 2 or more hours following ingestion and may be delayed for up to 48 hours or more. Over 75% of children with CMPA have **more than one** of the conditions listed in section 1.1.	Trial of a Cow's Milk Protein free diet - see CMPA algorithm. 10% of children with CMPA either do not respond to an Extensively Hydrolysed Formula (EHF) or respond and later relapse. These children require a formula based on amino acids- see CMPA algorithm (AFF). In addition to a vitamin D supplement, a calcium supplement is recommended for breast feeding mothers following a milk free diet. The calcium requirements for lactating mothers are approximately 1250mg of calcium/day. If mother is not taking adequate milk free alternatives then a prescription may be required. If there is no clear improvement cow's milk protein should be re-introduced into the child's diet. A guide on re-introducing cow's milk after initial trial is outlined on page 7.	Amino Acid formulae should only be prescribed; • According to the CMPA algorithm or • On recommendation of a paediatrician or dietitian. Lactose free milks contain cow's milk protein and are **not** suitable.

3.2. Lactose Intolerance

Notes[1,2]	Treatment	Prescribing Notes
It is not classed as an allergy but rather intolerance. It is not common. **Primary lactose intolerance** can arise as a result of an inherited deficiency of lactase, the enzyme needed to digest lactose. **Secondary lactase deficiency** may occur as a result of either: • Post-gastroenteritis infection (usually transient) or • Secondary to CMPA when there are on-going effects of undiagnosed Non-IgE CMPA.	**Post-gastroenteritis infection** If diarrhoea persists beyond 14 days consider **trial of a lactose-free diet**. A positive response usually occurs within **48 hours**. If there is improvement, continue diet for 6 weeks. After 6 weeks re-introduce lactose containing milk.	There is **no support** for using a partially hydrolysed, low lactose formula such as Comfort® milks. **If CMPA suspected;** Lactose-free formula or Colief® drops **must not be prescribed** as it is likely obscure the correct diagnosis of CMPA.

3.3. Colic

Notes[1]	Treatment	Prescribing Notes
Definition: Inconsolable crying with limb flexure in an otherwise healthy, thriving infant, which lasts for more than 3 hours per day, occurs on 3 or more days per week, has persisted for more than 3 weeks starting in the first weeks of life and ceasing around 3 to 4 months of age. It occurs in both formula fed and breast fed infants and affects up to 20% of infants. The causes are poorly understood however there is no good evidence that it is caused by either lactose in the diet or excess intestinal gas. Approximately 10% of infants with infantile colic may have CMPA particularly when there is a positive history of atopic eczema, allergic rhinitis, asthma or food allergy in a 1st degree relative (mother, father, or siblings) or the symptoms listed on page 4/5.	Where CMPA suspected consider a **2 week diagnostic trial excluding** of cow's milk protein. Planned reintroduction of cow's milk protein, either into the mother's diet (if breast fed) or as formula (if formula fed) see page 7. See CMPA algorithm.	**There is no support for prescribing;** • Colief® • A partially hydrolysed, low-lactose formula • A lactose-free formula • Infacol® or Dentinox Colic Drops® (Simeticone)

3.4. Gastro - Oesophageal Reflux (GOR)/ Gastro - Oesophageal Reflux Disease (GORD)

Notes[1]	Treatment	Prescribing Notes
GOR Defined as: 'The effortless passage of gastric contents into the oesophagus with or without **regurgitation** or **vomiting'.** It is a normal physiological process often occurring several times a day in healthy infants and is not thought to be uncomfortable. Intercurrent infections will always worsen GOR temporarily. It occurs in both formula fed and breast fed infants and should resolve spontaneously in most infants by 12 to 14 months of age and often earlier.	Check for overfeeding childs 0 to 6 months need around 150mL/kg/day of formula. Offer a trial of smaller, more frequent feeds (while maintaining an appropriate total daily amount of milk) **Then** Consider a 2 week trial of thickened feeds. Either; • Infant Gaviscon sachets • Formula milk with added Carobel® or • Anti-regurgitation formulae (for example, containing rice starch, cornstarch, locust bean gum or carob bean gum). Larger holed teats will be needed.	**Do not prescribe** Anti Reflux formulae **along with** other thickening agents such as Carobel® or Gaviscon® Child sachets as this could lead to over-thickening of the stomach contents. Anti-regurgitation child formulas require an acid environment in order to thicken and therefore will not work properly when prescribed along with antacid medications such as omeprazole.
GORD When the reflux of the gastric contents is thought to cause troublesome symptoms and/or complications in infants: • Recurrent and significant regurgitation, vomiting +/- with faltering growth. • Oesophagitis symptoms – irritability, back-arching, hiccups, feeding aversion, blood in refluxate. • Possible associated lower airway signs – apnoea, wheezing, recurrent infection, even acute life-threatening events.	A 2 week trial of omeprazole may be considered. Refer to guidance Guidance on Oral/Enteral Proton Pump Inhibitor (PPI) Selection and Administration (For Children) In a small number of infants CMPA may be considered if not responsive to all other treatments and especially if there is a family history of atopic allergy. Consider a 4 week trial - 2 minimum of milk free diet. See CMPA algorithm.	

4. Resources To Be Used With The Guidance

- Cows Milk Protein Allergy PIL.pdf: Advice for parents and carers whose children may have cow's milk protein allergy.
- Milk free weaning: Advice for parents and carers whose children have cow's milk protein allergy - Cows Milk Protein Allergy - Milk Free Weaning PIL.pdf
- Milk ladder, Guidance and Recipes - iMAP milk ladder

5. References And Further Information

1) T. Brown, *et al,* (2017) Better recognition, diagnosis and management of non-IgE-mediated cow's milk allergy in infancy; iMAP- an international interpretation of the MAP (Milk Allergy in Primary Care) guideline. *Clinical and Translational Allergy* 2017 **7**:26
2) NICE Clinical Guideline 116 Food Allergy in children and young people www.nice.org.uk/guidance/CG116
3) S. Koletzko, *et al*, (2012) Diagnostic Approach and Management of Cow's- Milk Protein Allergy in Infants and Children: ESPGHAN GI Committee Practical Guidelines. JPGN 2012;55: 221–229).
4) Department of Health and Social Care and the UK Committee for UNICEF, NHS Better Start For Life, Guide to bottle feeding, 2022 Bottle feeding leaflet
5) Royal Aberdeen Children's Hospital (RACH) Guidance on Oral/Enteral Proton Pump Inhibitor (PPI) – Version 2, J Smith, RACH Pharmacy Department, September 2024 - Reviewed by Paediatric Gastroenterology Team - (Adapted from NHS Tayside Guidance for PPI selection for children with GORD)

6. Key Contacts

- Paediatric Dietitians, Aberdeen, 01224 552630 - gram.referdietpaeds@nhs.scot
- Community Dietitians, Aberdeen, 0345 0990 200 - gram.referdietpaeds@nhs.scot
- Dietetic Department, Moray, 01343 567350 - gram.moraydietitians@nhs.scot

7. Consultation List

Tracy Cameron	Joint Lead Paediatric Dietitian, Royal Aberdeen Children's Hospital
Fay Clayton	Infant feeding coordinator Aberdeenshire
Katy Ker	Joint Lead Paediatric Dietitian, Royal Aberdeen Children's Hospital
Rachel Semple	Paediatric Dietitian, Royal Aberdeen Children's Hospital
Elizabeth Stevenson	Paediatric Dietitian, Moray
Ailsa Wildgoose	Grampian Dietetic Prescribing Advisor
Dr Adrian Crofton	Lead Clinician, Torry Medical Practice, Executive Director, River Dee Medical Group
Dr Lindsay Grant	GP, Calsayseat Medical Practice

Aberdeen City Health Visiting teams
Aberdeenshire Health Visiting teams
Moray Health Visitor teams
Gastroenterology specialist team - Royal Aberdeen Children's Hospital

8. Distribution List

General Practitioners
Health Visitor Leads
Midwife Leads
Neonatal Unit Consultant Paediatric
Nursing Leads
NHS Grampian Dietitians