

# Information for Clinicians

## Paediatric Department

### Cow's Milk Protein Allergy: Diagnosis and Management in Infants

This guidance is designed to be used by all health care professionals involved in the care of infants and young children with suspected Cow's Milk Protein Allergy (CMPA).

It has been developed by Consultant Paediatricians and Paediatric Dietitians from Royal United Hospitals Bath NHS Foundation Trust (RUH), Great Western Hospitals NHS Foundation Trust (GWH) and Salisbury Foundation Trust (SFT) in conjunction with the local CCG Medicines Management Team.

It includes further information on:

- Differentiation between IgE and non-IgE Allergy
- Distinction between lactose intolerance and CMPA
- Assessment and diagnosis of CMPA (*pages 2, 3 and flowchart p4*)
- Ongoing management of CMPA (*page 5*)
- Different types of formula milk (*pages 6-8*)
- Prescribing guide for quantities of formula & transition to non-specialist formula (*pages 8-9*)
- Patient/family information leaflets (*pages 6 & 9*)

### Milk Allergy: Background:

Milk allergy is common in infants although in the majority it will resolve with age. The symptoms of milk allergy can be non-specific and many of the typical symptoms also occur in well babies without CMPA. Accurate assessment is important to allow prompt relief of symptoms for those affected but also to avoid over-diagnosis leading to unnecessary exclusion diets.

#### Non-IgE mediated Allergy (delayed):

- The majority of infants with milk allergy have non-IgE milk allergy
- Non-IgE milk allergy is also termed 'delayed onset' or type 2 allergy
- Non-IgE allergy is sometimes referred to as milk intolerance although this term can include other non-allergic symptoms from milk
- Symptoms occur between 2-48 hours or longer after exposure
- Mechanism uncertain but thought to occur due to T-cell activation and localised antibodies in the gut or other tissues. There are no accurate laboratory tests available for clinical use to diagnose non-IgE allergy

#### IgE mediated Allergy (immediate):

- A smaller group of infants have IgE-mediated, sometimes termed 'acute onset' or type 1 allergy
- Symptoms usually occur within minutes, sometimes up to 2 hours after exposure

## Initial Assessment:

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Symptoms of mild milk allergy are common in otherwise well infants or those with other diagnoses. There should however be increased suspicion of milk allergy in infants with multiple, persistent or treatment-resistant symptoms (e.g. reflux not responding to smaller feeds & feed thickeners; eczema not responding to frequent emollients +/- hydrocortisone).

There is overlap between the symptoms of non-IgE and IgE mediated milk allergy but an 'allergy focused history' can help to distinguish the two groups (see **NICE guideline CG116** for further information)

*Differentiation of the two groups is important as management is different*

### Questions which may be helpful are:

#### Milk feeds:

Was/is the child breast-fed? duration / partial / exclusive?

If exclusively breastfed: maternal dietary intake / foods?

If formula/mixed: age when formula / milk introduced, which formula milk?

#### Weight gain:

History of failure to gain weight

#### Dietary history from birth:

What food groups are eaten and any reaction(s)? Ask about age of onset of symptoms /

Frequency / consistency of reaction(s)

Appetite / do they eat well / enjoy food?

Any food(s) avoided?

#### Family history, ask if

Parents have allergic disease e.g. asthma, hayfever

Either parent avoids certain foods

If 'yes', why?

#### Symptoms and reactions:

What are the symptoms of concern?

What is their severity? Ask for a thorough description of the most recent reaction. Ask about age of onset of symptoms / frequency / consistency of reaction(s)

#### Management of previous reactions to food:

**Ask about:** Symptoms resolved without specific / medical intervention

Medication given / which route / time from treatment to recovery

## Milk-free diet

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Mammalian milks (e.g. Goat's milk, sheep's milk etc.) have similar proteins to cow's milk so all need to be excluded at least initially. Some infants will be sensitised to the small quantities of cow's milk proteins which get into breast milk from maternal diets.

**Milk allergy is due to an immune reaction to milk protein, not a reaction to lactose which is the main sugar in milk**

## Principles of Management

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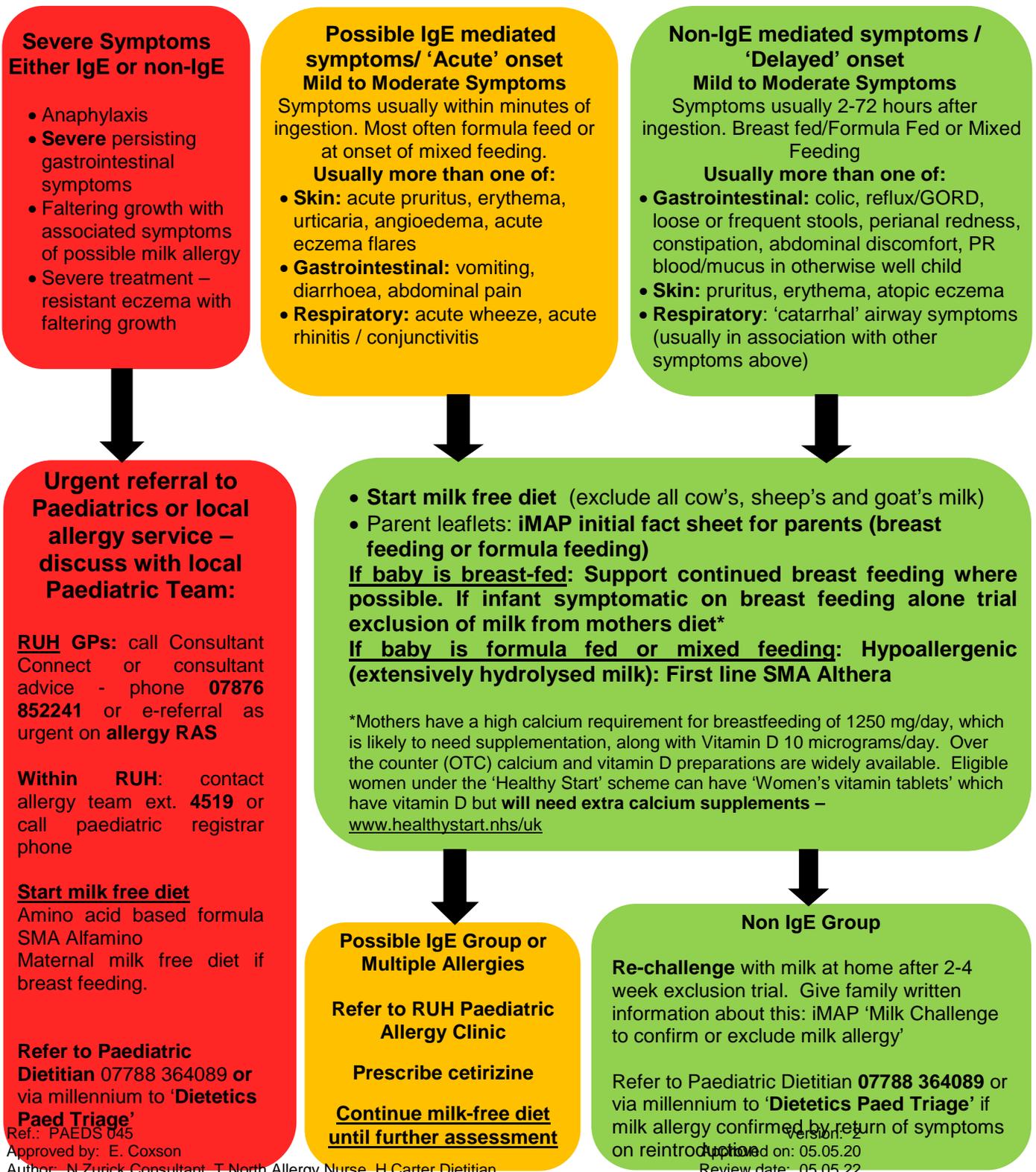
- **Initial management includes commencing a milk-free diet. Breast feeding mothers should be supported to continue.** If symptoms have occurred whilst the baby is exclusively breast-fed, or if significant symptoms persist when mixed-feeding, a trial of a maternal milk-free diet should be advised.
- **Those with severe symptoms and those with possible IgE mediated allergy** should continue a milk free diet and be referred for allergy testing and further assessment.
- **Exclusion and reintroduction trials for non-IgE mediated symptoms:** reintroduce milk into diet after short (2-4 week) exclusion trial. Symptoms of non-IgE allergy usually respond very quickly to milk exclusion (most often within 72hrs). Reintroduction only has to be for long enough to be confident that the symptoms have returned, not a set time.
- There is a **risk of over-diagnosis** if mild, transient or isolated symptoms are over-interpreted or if milk exclusion diets are not followed with a **reintroduction challenge**.
- **There is no validated test for non-IgE mediated milk allergy except exclusion diet followed by a reintroduction challenge.**
- Those with possible IgE mediated symptoms should be prescribed **antihistamine** for use as required (preferably cetirizine, including for those under 1 year of age. (See RUH Antihistamine leaflet PAE063 for more information )

## Lactose Intolerance

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- Relatively uncommon in infants except as a temporary problem after gastroenteritis; it does not cause rashes, eczema etc.
- Caused by a deficiency of the enzyme 'lactase' which digests the milk sugar element of milk and is **NOT** an allergy
- Lactose free formula products can be bought at a similar cost to standard infant formula and should **NOT** be supplied on FP10 prescription. Most pharmacies can order supplies for next day delivery
- There is separate guidance available:  
[www.ruh.nhs.uk/patients/services/clinical\\_depts/paediatrics/documents/patient\\_info/PAE030\\_Lactose Free diets.pdf](http://www.ruh.nhs.uk/patients/services/clinical_depts/paediatrics/documents/patient_info/PAE030_Lactose_Free_diets.pdf)

## Initial Assessment of Suspected Cow's Milk Allergy in Infants



**Severe Symptoms  
Either IgE or non-IgE**

- Anaphylaxis
- **Severe** persisting gastrointestinal symptoms
- Faltering growth with associated symptoms of possible milk allergy
- Severe treatment – resistant eczema with faltering growth

**Possible IgE mediated symptoms / 'Acute' onset  
Mild to Moderate Symptoms**  
Symptoms usually within minutes of ingestion. Most often formula feed or at onset of mixed feeding.  
**Usually more than one of:**

- **Skin:** acute pruritus, erythema, urticaria, angioedema, acute eczema flares
- **Gastrointestinal:** vomiting, diarrhoea, abdominal pain
- **Respiratory:** acute wheeze, acute rhinitis / conjunctivitis

**Non-IgE mediated symptoms / 'Delayed' onset  
Mild to Moderate Symptoms**  
Symptoms usually 2-72 hours after ingestion. Breast fed/Formula Fed or Mixed Feeding  
**Usually more than one of:**

- **Gastrointestinal:** colic, reflux/GORD, loose or frequent stools, perianal redness, constipation, abdominal discomfort, PR blood/mucus in otherwise well child
- **Skin:** pruritus, erythema, atopic eczema
- **Respiratory:** 'catarrhal' airway symptoms (usually in association with other symptoms above)

**Urgent referral to Paediatrics or local allergy service – discuss with local Paediatric Team:**

**RUH GPs:** call Consultant Connect or consultant advice - phone **07876 852241** or e-referral as urgent on **allergy RAS**

**Within RUH:** contact allergy team ext. **4519** or call paediatric registrar phone

**Start milk free diet**  
Amino acid based formula SMA Alfamino  
Maternal milk free diet if breast feeding.

**Refer to Paediatric Dietitian 07788 364089 or via millennium to 'Dietetics Paed Triage'**

- **Start milk free diet** (exclude all cow's, sheep's and goat's milk)
- Parent leaflets: **iMAP initial fact sheet for parents (breast feeding or formula feeding)**

**If baby is breast-fed:** Support continued breast feeding where possible. If infant symptomatic on breast feeding alone trial exclusion of milk from mothers diet\*

**If baby is formula fed or mixed feeding:** Hypoallergenic (extensively hydrolysed milk): **First line SMA Althera**

\*Mothers have a high calcium requirement for breastfeeding of 1250 mg/day, which is likely to need supplementation, along with Vitamin D 10 micrograms/day. Over the counter (OTC) calcium and vitamin D preparations are widely available. Eligible women under the 'Healthy Start' scheme can have 'Women's vitamin tablets' which have vitamin D but **will need extra calcium supplements** – [www.healthystart.nhs.uk](http://www.healthystart.nhs.uk)

**Possible IgE Group or Multiple Allergies**

**Refer to RUH Paediatric Allergy Clinic**

**Prescribe cetirizine**

**Continue milk-free diet until further assessment**

**Non IgE Group**

**Re-challenge** with milk at home after 2-4 week exclusion trial. Give family written information about this: iMAP 'Milk Challenge to confirm or exclude milk allergy'

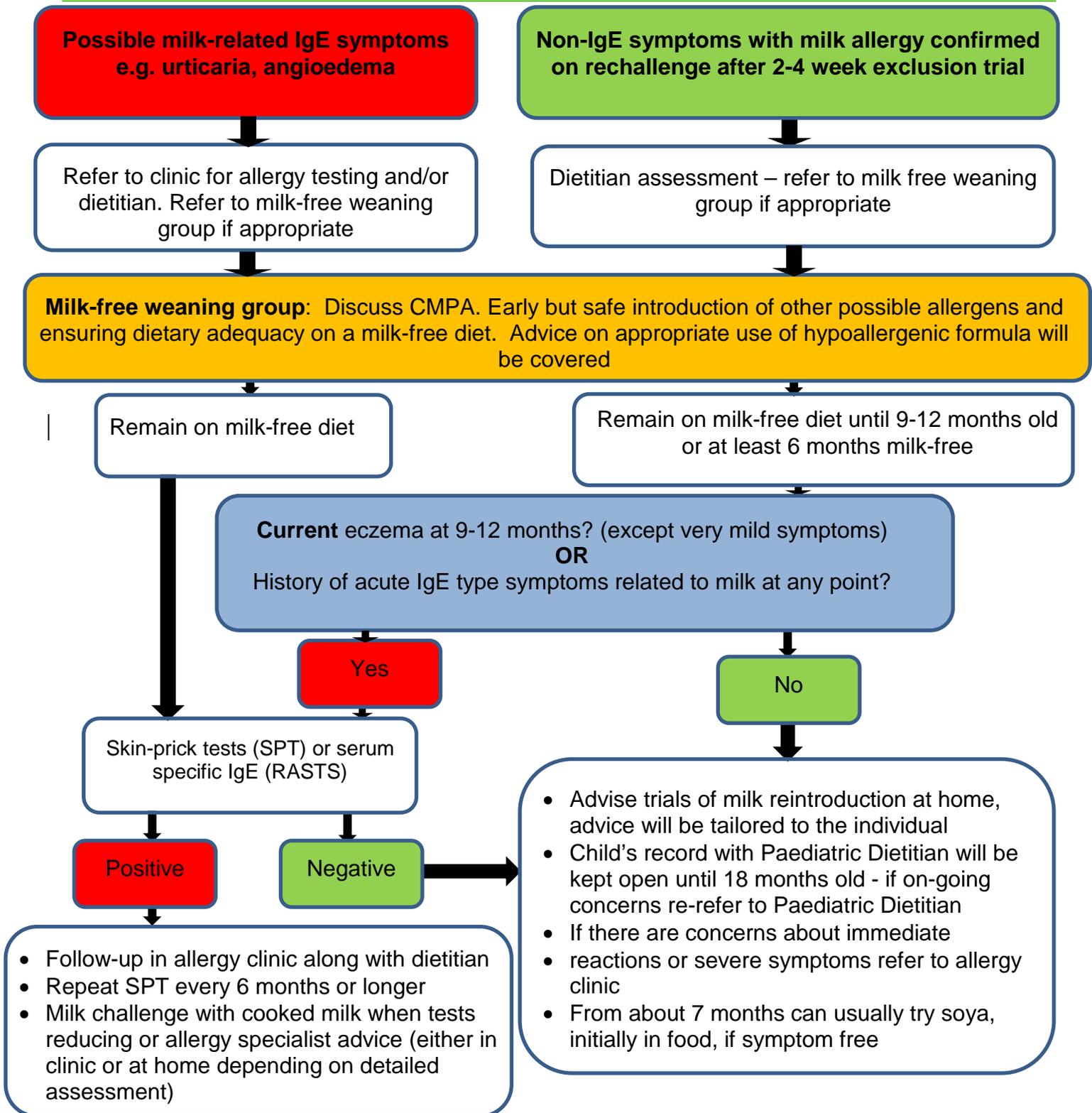
Refer to Paediatric Dietitian **07788 364089** or via millennium to '**Dietetics Paed Triage**' if milk allergy confirmed by return of symptoms on reintroduction

Ref.: PAEDS 045  
Approved by: E. Coxson  
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Date of Issue: May2020

Version: 2  
Updated on: 05.05.20  
Review date: 05.05.22  
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**If no improvement in symptoms when milk excluded, consider other diagnoses. If milk allergy still highly suspected consider a trial of amino acid formula e.g. SMA Alfamino**

## On-going management of Milk Allergy



**Supporting information:** please provide parents and carers with the following leaflets as appropriate: These are on the RUH webpages and iMAP leaflets can be found at:

<https://gpifn.org.uk/imap/>

- iMAP initial fact sheet for parents or RUH 'Could it be milk allergy – exclusion trials' leaflet
- iMAP leaflet for breastfeeding parents
- iMAP Milk challenge information sheet
- RUH Leaflet – Reintroduction of milk to your child's diet (this ladder is more suitable for those with severe symptoms)
- RUH Leaflet – Milk free diets
- RUH Leaflet – Calcium for your child

## Types of Infant Formula and Milks

### Hypoallergenic Infant Milks

- An extensively hydrolysed formula (eHF) will be appropriate for nearly all cows' milk allergic infants. In eHF the cow's milk protein has been broken down into small peptides.
- Inform the family that these milks have an unusual smell and taste but that most babies will tolerate them. There is no clear difference in taste tolerance between the various brands.
- If there is any difficulty getting the baby to take the eHF try the following
  - Breast fed infants requiring top-ups – eHF can initially mixed with expressed breast milk
  - For those with non-IgE symptoms, the eHF can be mixed with the infant's normal formula until the baby is used to it
  - Make sure family are offering the milk in a positive manner – babies will pick up on signals if parents make it clear they think the milk tastes disgusting!
  - For older babies use a lidded cup or a bottle not an open cup.
- If the first eHF prescribed is refused (taste acceptability only relevant for 6-12months) – ask for dietitian advice or try an alternative eHF. If symptoms persist then trial Amino-Acid based formula (AAF)
- Breast milk has a higher percentage of whey proteins than cow's milk. All the whey based extensively hydrolysed formulas on UK market contain lactose: this is not clinically important for most infants unless they have significant enteropathy.
- If both cow's milk and soya allergic, infants will often need to continue hypoallergenic milk (eHF or AAF) until 18 months or older. The Paediatric Dietitian will advise if it can be stopped sooner.

## First Line eHF milk suitable from birth = SMA Althéra (Nestle Health Science)

- **Alternative options if not tolerated or advised by dietitian / allergy specialist:**
  - **Nutramigen** (Mead Johnson) with LGG 1 (from birth) 2 (from 6 months)
  - **Aptamil Pepti** (Milupa) 1 (from birth) 2 (from 6 months) Pepti is the least hydrolysed eHF
  - **Similac Alimentum** (Abbott Nutrition) from birth

*Hypoallergenic milks where the fats are also altered e.g. Pepti-Junior (Cow & Gate) and Pregestimil (Mead Johnson) are aimed at gastrointestinal disorders such as short gut where there is also fat malabsorption so are not first line for cow's milk allergy where fat absorption is not a problem*

## Amino-Acid based formula (AAF) suitable from birth.

### First Line = SMA Alfamino (Nestle Health Science)

- A small number of infants will need an amino acid based formula (elemental formula) but this should usually be prescribed on the advice of a Consultant Paediatrician, Allergy Specialist or Paediatric Dietitian
- AAF are significantly more expensive than eHF
- AAF are first line for those who have had **anaphylaxis** to milk or who have significant enteropathy e.g. persistent water diarrhoea and faltering growth. They are sometimes recommended if top-up feeds are needed if the baby was getting significant symptoms related to maternal milk intake when breast fed

### Alternative options if not tolerated or as advised by dietitian / allergy specialist:

- **Neocate LCP** (Nutricia) from birth to one year, can be used beyond if appropriate or **Neocate Junior** (Nutricia) for over one year. **Neocate Syneo** is Neocate LCP with added pre and probiotics and may be recommended for severe GI symptoms in some cases.
- **Nutramigen Puramino** (Mead Johnson) from birth

## Soya based formula and milks

- Should not be used as first line for babies under 6 months as there is a high chance of cross reactivity in that age group
- Theoretical concerns about phytate levels which may reduce nutrient absorption in very young babies and about phytoestrogen levels found in soya milk
- Soya formula should **NOT** be prescribed, as it is available commercially
- Soya formula can be used in babies over 6 months if extensively hydrolysed milk (eHF) is refused by the baby.
- Babies with CMPA can usually try soya in solid food from about 7 months and then increase amount as tolerated. If tolerated, change to soya milk from approx. 12 months of age (**Alpro Growing Up Soya Drink 1-3+** or as infant formula). Adult soy milks can be used in small amounts for cooking etc. provided it is fortified with calcium.

## Other milks

Most milk substitutes are highly fortified with calcium (120mg per 100g) apart from the 'organic' products

### Fortified calcium Oat milk

- Can be used from six months old in cereal and in cooking and as a milk replacement after 12 months old, if child is not able to tolerate soya milk. It has a lower protein content than soya and prescribable milks

### Nut milks, coconut based milks etc.

- Should **NOT** be used as a main milk drink for under 2 year olds unless advised by dietitian /allergy specialist, as their protein, energy and vitamin content is low. They can be used in in cooking, on cereals etc.

### Sheep and Goat's milk

- Milk and infant formula based on these milks contain similar proteins to cow's milk and should also be **excluded**. They are sometimes tolerated relatively early during the reintroduction phase when the allergy is improving and by some children with non-IgE milk symptoms e.g. eczema

### Lactose free milk / formula

- (e.g. SMA Lactose free, Aptamil Lactose free) is **NOT** suitable for treatment of symptoms of milk allergy as the protein is unaltered (see separate guidelines on lactose intolerance in childhood). Lactose free formula should **NOT** be prescribed as it is available commercially

### Rice milk

- Is **NOT** advised for under 5 year olds (due to arsenic levels which may theoretically increase future cancer risk)

## Prescribing Infant Formula and Milks

When introducing a specialist formula only prescribe 3 x 400g/450g tins as a trial in case there are tolerance issues

Age	Average infant formula intake / 24 hours	Total average amount per 24 hour	Tins per month required
0-2 months	90ml – 120ml (3-4floz) x 6-8 feeds	630 – 780 ml (21-26floz)	8 x 400g/450g tins 4 x 900g tin
3-6 months	180ml (6floz) x 5 feeds	900 – 1050ml (30-35floz)	12 x 400g/450g tins 6 x 900g tin
7-11 months	210ml (7floz) x 3 feeds	630ml (21floz)	8 x 400g/450g tins 3 x 900g tins
12-18 months*		300ml (10floz)	4 x 400g/450g tins 2 x 900g tins

\*Prescriptions should not be issued for children over the age of 18 months unless Consultant Paediatrician / Allergy team or Paediatric Dietitian request it is continued.

## Transition from specialist formula

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Most infants with a cow's milk allergy will be able to come off specialist formula shortly after 12 months of age **if** they are able to tolerate soya based milks. Some infants will move to a soya based formula before 12 months but for others the transition will be more difficult, particularly if they have other allergies. Soya in solid foods can usually be tried from around 7 months old.

Parents should be informed their prescription will be discontinued by 18 months unless advised to continue by allergy team. It can be explained that there are now a wide range of milk and soya free milk alternatives available, such as oat, nut and coconut based milks. **Families should be advised to check they are fortified with calcium.**

If taste is a problem then parents can add small amounts of the prescribed formula and introduce the taste slowly. Vanilla essence or dairy-free milkshake powders can also be used at first to introduce the change in taste provided dental hygiene advice is followed. If a child takes their prescribed milk from a bottle then this is the right opportunity to give the new drink in a beaker or cup.

Nationally it is advised that all children under five are given a vitamin supplement to provide vitamins A, C, and D if they are breast fed or drinking less than 500ml of formula per day. These should be purchased by the parent unless they are entitled to Healthy Start Vitamins ([www.healthystart.nhs.uk](http://www.healthystart.nhs.uk))

## Information Leaflets

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The RUH has a number of related leaflets: these are all on the RUH intranet and can be downloaded by families and GP's from the RUH external website:

- Milk allergy diagnosis for babies (how to safely do a milk free trial in babies)
- Milk free diet factsheet
- Reintroduction of milk into your child's diet
- Diet and eczema
- Antihistamines
- Calcium in your child's diet

For further advice, please contact your local Allergy team or Paediatric Dietitian (appendix 1)

## References

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The Milk Allergy in Primary Care (MAP) Guideline 2019: <https://gpifn.org.uk/imap/>  
Diagnosis and management of non-IgE-mediated cow's milk allergy in infancy - a UK primary care practical guide, C. Venter, T. Brown, N. Shah, J. Walsh and A. Fox, Clinical and Translational Allergy 2013, 3:23 <http://www.ctajournal.com/content/3/1/23>

BNF for Children 2018-2019

NICE guidance CG116 Food allergy in children and Young People February 2011  
<http://www.nice.org.uk/cg116>

NICE Cow's milk allergy in children: Summary December 2019 - <https://cks.nice.org.uk/cows-milk-allergy-in-children#!topicSummary>

BSACI guideline for the diagnosis and management of cow's milk allergy, D. Luyt, H. Ball, N. Makwana, M. R. Green, K. Bravin, S. M. Nasser and A. T. Clark, Clinic & Experimental Allergy, 2014: 44, 542-672 <https://onlinelibrary.wiley.com/doi/pdf/10.1111/cea.12302>

## Appendix 1

### Referrals to Paediatric Allergy Clinic RUH:

Referrals from GPs via NHS e-referral 'RUH Allergy referral assessment service' (RAS)

Consultants, Dietitians, Health visitors and other AHPS can refer via e-mail:  
[ruh-tr.paediatricallergy@nhs.net](mailto:ruh-tr.paediatricallergy@nhs.net)

Allergy Nurse Specialist phone: 01225 824519

Dietitian referrals: 07788 364089 or via within RUH via Millennium to 'Dietetics Paed Triage'

## Amendment History

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Issue	Status	Date	Reason for Change	Authorised
		May 2020	Updated in line with latest iMAP guidance and in conjunction with surrounding Trusts/CCG	N Zurick & paediatric dietitians

Ref.: PAEDS 045  
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