

Cow's Milk Protein Allergy (CMPA) Diagnosis and Management in Infants

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

The 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 includes further information on:

- Differentiation between IgE and non-IgE Allergy
- Distinction between lactose intolerance and CMPA
- Assessment and diagnosis of CMPA
- Ongoing management of CMPA
- Different types of formula milk
- Prescribing guide for quantities of formula
- Patient information leaflets
 - The iMAP initial fact sheet for parents
 - iMAPleaflet for breastfeeding parents
 - iMAPMilk Challenge to confirm or diagnose mild or moderate Cow's Milk Protein Allergy
- Contact details for Paediatric Dietitians
(Note: separate forms for BANES, GWH & WHC)

Milk Allergy: Diagnosis and Management in Infants

Milk allergy is common in infants although in the majority it will resolve with age. The symptoms of milk allergy can be non-specific. 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:

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 related 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 or siblings 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

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

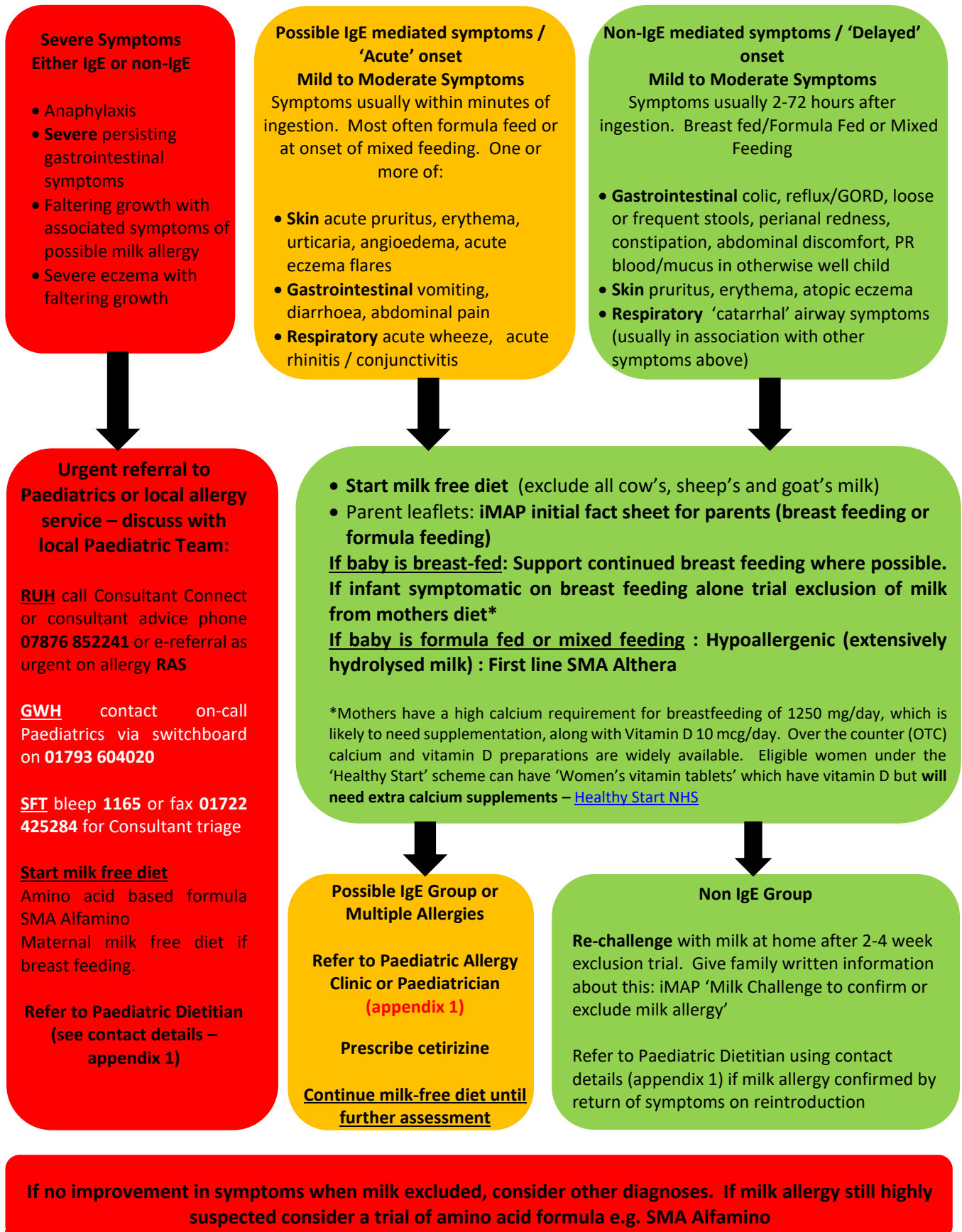
- **Initial management includes commencing a milk-free diet.** Breast feeding mothers should be supported to continue. If symptoms have occurred whilst the baby is exclusively breast fed, or if significant symptoms persist when mixed-feeding a trial of a maternal milk-free diet should be advised.
- **Those with severe symptoms and those with possible IgE mediated allergy** continue a milk free diet and refer for allergy testing and further assessment.
- **Exclusion and Reintroduction for non-IgE mediated symptoms:** reintroduce milk into diet after short (2-4 week) exclusion trial.
- 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 online for more information)
https://www.ruh.nhs.uk/patients/services/clinical_depts/paediatrics/documents/patient_info/PAE063_Antihistamine_Allergy.pdf

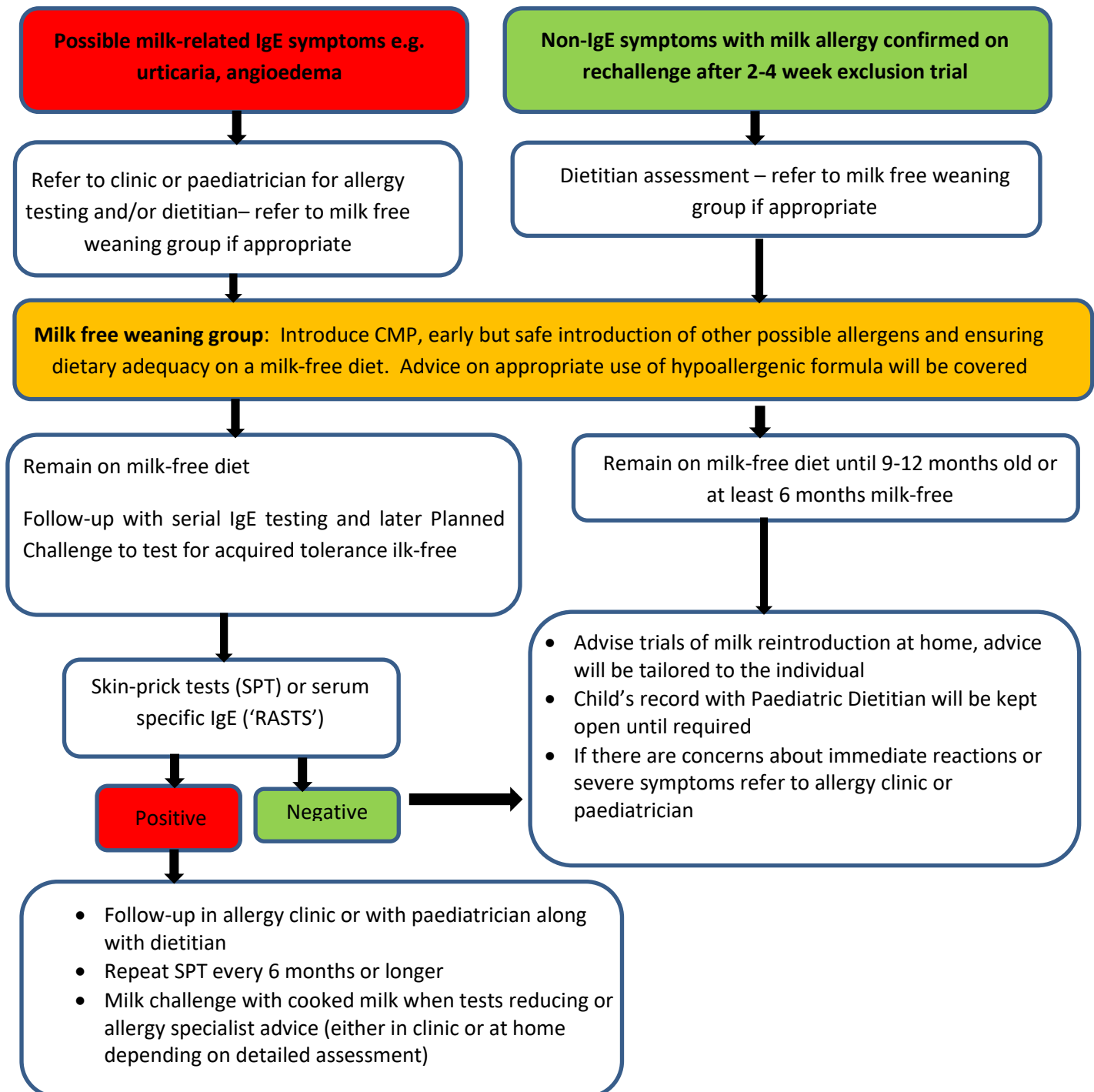
Lactose Intolerance

- 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

From the history put into one of the three groups below





From about 7 months can usually try soya initially in food, if symptom free

Supporting information: please provide parents and carers with the following leaflets

- iMAP initial fact sheet for parents https://gpifn.files.wordpress.com/2019/10/imap_patient_factsheet_original.pdf
- iMAP leaflet for breastfeeding parents <https://gpifn.files.wordpress.com/2019/10/imap-supporting-breastfeeding-factsheet.pdf>
- Milk challenge information sheet [The Early Home Reintroduction to Confirm the diagnosis of Cow's milk allergy](https://www.bda.uk.com/resource/calcium.html)
- Allergy UK milk free diet for babies and children <https://www.allergyuk.org/information-and-advice/conditions-and-symptoms/469-cows-milk-allergy>
- BDA Calcium Food Fact sheet <https://www.bda.uk.com/resource/calcium.html>

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 significant 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 taste 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 have significant enteropathy.

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

- **Alternative options if not tolerated or advised by dietitian/ allergy specialist:**
 - **Aptamil Pepti (Milupa)** 1 (from birth) 2 (from 6 months)- the least hydrolysed eHF
 - Lactose Free options:
 - **Alimentum** (Similac Abbott Nutrition) from birth **Nutramigen** (Mead Johnson) with LGG 1 (from birth) 2 (from 6 months) Nutramigen 3 for over 12 months
- 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 usually first line for cow's milk allergy where fat absorption is not a problem

First Line Amino-Acid based formula (AAF) from birth = **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 watery 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 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
 - **Elecare (Similac Abbot Nutrition)** from birth

Soya based formula and milks

- **Should not be** used as first line for babies under 6 months as there is a high change 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. Can be used in babies over 6 months if extensively hydrolysed milk (eHF) is refused by the baby. 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

If both cow's milk and soya allergic, infants will need to continue hypoallergenic milk (eHF or AAF) until 18 months or older. Paediatric Dietitian will advise if it can be stopped sooner

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 not high enough. They can be used in small amounts in cooking 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 or by some children with non-IgE milk symptoms e.g. eczema
- **Lactose free formula**
 - (e.g. SMA Lactose free, Enfamil LF) 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)

Types of Infant Formula and Milks

To introduce 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 Paediatricians or Paediatric Dietitian request it is continued

Transition from specialist formula

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.

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 milk shake 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 can be purchased by the parent unless they are entitled to Healthy Start Vitamins (www.healthystart.nhs.uk)

The RUH has a number of related leaflets: there 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

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

References

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>

BNFc online – <https://bnfc.nice.org.uk/>

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. Referral information and contact details



Royal United Hospitals Bath
NHS Foundation Trust

**Paediatric Dietitians,
Nutrition & Dietetic Services,
Royal United Hospitals Bath NHS Foundation Trust
Combe Park
Bath BA1 3NG**

or email it to: ruh-tr.paediatricdieteticreferrals@nhs.net

Please note that this email address is for referrals only.
If the referral is urgent please telephone the Dietetic
Department on **01225 826449**.

Specialist Allergy Clinic Royal United Hospital (RUH)

ruh-tr.paediatricallergy@nhs.net

This mailbox is specifically for queries from healthcare professionals. GP referrals should go via Choose and Book/ E-referral service. Allergy RAS FOR PARENT QUERIES OR SUPPORT use ruh-tr.childrensallergyclinic@nhs.net PLEASE ensure all emails have the patients full name and either date of birth or hospital/NHS number This mailbox is monitored regularly - but due to current short-staffing it may take us 1-2 weeks to reply. For very urgent queries please contact our allergy secretary Maria on 01225 824393



Great Western Hospitals
NHS Foundation Trust

- **Referral to GWH Paediatric Dietitians** refer via email gwh.paediatricdieteticreferrals@nhs.net
- **Paediatric Consultants** Contact via Consultant Connect



Wiltshire Health & Care Community Paediatric Dietetics

Nutrition and Dietetics Chippenham Community Hospital, Chippenham, Wiltshire SN15 2AJ
Telephone: Chippenham office: 01249 456512/Salisbury office: 01722 429333

- Telephone support
- Outpatient and remote clinics (telephone and video)
- Monthly cow's milk protein allergy (CMPA) education groups in Chippenham and Salisbury

Referrals are accepted from health professionals; to include Acute Paediatricians, Community Paediatricians, GPs, Health Visitors and other Wiltshire Health & Care community health professionals.

Referrals can be sent via email: whc.wiltshiredietetics@nhs.net

SDH Paediatric Consultant referrals via email to sft.centralbooking.adminteam@nhs.net