Appropriate Prescribing of Specialist Infant Formulae

Purpose of the guidance

These guidelines aim to assist GPs and Health Visitors with information on the appropriate use of prescribable infant formula. The guidelines are targeted at infants 0-12 months. Some of the prescribable items mentioned can be used past this age, advice on this is included in the guidelines. The guidelines advise on:

- ✓ initiating prescribing
- ✓ quantities to prescribe
- ✓ which products to prescribe for different clinical conditions
- ✓ reviewing and discontinuing prescriptions
- ✓ when onward referral for dietetic advice and/or secondary/specialist care should be considered.

What is an allergy?

A food allergy is where the immune system recognises a protein in food (or molecule linked to a protein) as foreign to the body and triggers a response against it. Food allergies may be IgE-mediated or non-IgE mediated but mediated by other immune mechanisms. IgE-mediated reactions are acute and usually occur within 2 hours of ingesting the food. Non-IgE mediated reactions tend to be delayed and may occur up to 48 hours after food ingestion. See appendix two table 2 NICE 2011- Food Allergy in Children and Young People.

Food hypersensitivity is a reaction to proteins in foods, without any immune involvement in the reaction.

Lactose intolerance is a non-immune mediated response to the carbohydrate 'lactose' in cow's milk. There are 3 causes of lactose intolerance:

1. Congenital lactose intolerance is a congenital deficiency of the lactase enzyme responsible for metabolism of lactose. This is characterised by poor growth and infantile diarrhoea from first exposure to breast milk (which contains lactose).
2. Primary lactose intolerance- low levels of lactase, developed over a period of years but not before the ages of 2-5 years. Foods of lower lactose content will be tolerated.
3. Secondary lactose intolerance- temporary loss of lactase activity due to gastrointestinal illness damaging the small intestine e.g. viral gastroenteritis, giardiasis or coeliac disease. It is reversible by following a lactose free diet to allow the gut to recover for 6-12 weeks. Diagnosis is by clinical history and confirmed by exclusion of lactose-containing foods and subsequent improvement in symptoms.

Lactose free milks can be bought at a similar cost to standard infant formulae and should not routinely be prescribed. Patients can purchase low lactose formulae from their chosen retailer. However as they are less commonly used they may need to be ordered in specifically. In most cases stock can be obtained within a few working days.

Table One, over the next two pages describes the symptoms, actions and treatment options for both Non IgE Cows Milk Protein Allergy (CMPA) and IgE CMPA.

Table One

	Non IgE CMPA	IgE CMPA
Signs and Symptoms (one or more of)	• Usually occurs within the 1st year of life. • Atopic dermatitis • GI symptoms e.g. blood in stools, diarrhoea, vomiting, abdominal distension, colic, constipation • Persistent catarrhal airway symptoms, wheeze, runny nose, pallor • The more of the above symptoms involved the more likely the child is to have a milk allergy, particularly if different organs are affected or if the child has not responded to treatment for atopic eczema, reflux or chronic GI symptoms. • Breast fed infants can display similar symptoms due to milk protein from the mother's diet passing to the infant. • If treated effectively most children outgrow the allergy by 2 years. • Most children do not experience growth failure. • Symptoms can take hours – weeks to appear on exposure	• GI symptoms e.g. Acute vomiting or diarrhoea, faltering growth, refusal to eat. • Dermatological symptoms e.g acute worsening of eczema, uriticaria, pruritis, swelling of lips or eyes. • Respiratory symptoms e.g unexplained wheeze, rhinorrhoea, anaphylaxis, shortness of breath, cough, stridor. • Symptoms can take minutes – hours to appear on exposure.
Actions	• Elimination diet (4-8) weeks followed by a planned reintroduction challenge (to confirm diagnosis) • Refer to dietician for CMP exclusion diet • No need to refer to paediatrician if well controlled	• Refer to dietitian for CMP exclusion advice. • Refer to a paediatrician with a special interest in allergy for skin prick/RAST test.
Treatment – Initial	• Breast feeding is still the most appropriate choice of feed. The mother should follow a milk free diet and ensure sufficient calcium (1000mg per day), usually via a supplement. Symptoms should resolve within 2 weeks, if not it is unlikely that CMPA is the cause of symptoms. • Bottle fed infants require a hypo allergic formula, either extensively hydrolysed or amino acid. It is important to introduce one as soon as possible as formula vary in palatability. If not accepted initially, introduce by mixing with standard formula and slowly wean onto the hypoallergenic formula. **A minimum trial of 2 weeks is recommended,** if no improvement in symptoms after this time, the infant is unlikely to have CMPA.	• Breast feeding is still the most appropriate choice of feed. The mother should follow a diary free diet and ensure sufficient calcium (1000mg per day), usually via a supplement. • Bottle fed babies should be prescribed an amino acid formula. (0-12 months) • NICE UK food allergy guidelines state children with IgE allergy must not be challenged in community but instead lead by the paediatrician in the secondary care setting.
Treatment - Ongoing	• ***All infants with confirmed CMPA must be weaned onto a milk free diet and will require referral to the paediatric dietitian to advise on this and to***	• Prescribe on a two week basis and review every 3 months. • Prescription formula may be required beyond the age of 12 months on

	assess calcium intake as milk intake reduces. • All infants should be re-challenged with cow's milk between 12-18 months, depending on the time of diagnosis. Infants will require 6 months symptom free prior to a milk challenge. • By 2 years, all infants will be recommended to switch to normal cow's milk or if not tolerated, a commercially available substitute e.g. calcium enriched oat milk or soya milk. • Hypoallergenic formula should not be prescribed past 2 years unless specifically requested by the paediatric dietitian or paediatrician e.g. in cases of continued milk intolerance alongside faltering growth, or if child has multiple allergies including soya, oats, nuts	dietetic/paediatrician advice. Alternative milk supply must be established before the prescription of specialist formula is stopped.

Cow's milk protein may aggravate **gastroesophageal reflux** in some infants. Where reflux is suspected and not responding to anti-reflux treatment, a 2 week trial of an extensively hydrolysed formula may be considered. Where there is no improvement in reflux symptoms within 2 weeks, it is unlikely that milk protein is impacting on reflux and the formula should be stopped.

Where infants with GOR respond to milk free formula, they should initially be weaned onto a milk free diet and referred to a specialist dietitian for support. Where GOR is the primary concern it may be possible to challenge infants with milk solids between 8 and 10 months to confirm if milk free formula continues to be indicated. This should be monitored by a specialist dietitian.

Prescribing Options for non IgE CMPA

See Appendix 1.

- **Extensively hydrolysed** formulas are a hypoallergenic formula that is suitable for the vast majority of babies with cow's milk protein allergy. The cow's milk proteins in these formulas have been broken down considerably into very short chains, so they're no longer recognised by the immune system as whole cow's milk proteins and are unlikely to cause an allergic reaction. Extensively hydrolysed formulas are effective in at least 90% of infants with cow's milk allergy.
- **Amino acid** formulas are a hypoallergenic formula designed for the small number of babies with cow's milk allergy who have tried an extensively hydrolysed formula that has been recommended by a healthcare professional and still notice symptoms, or who have severe allergic reactions or multiple food allergies. Amino acid-based formulas don't contain any protein chains at all – they only use the basic building blocks of protein – amino acids, so they're unlikely to trigger an allergic reaction even in babies who are severely allergic.

Amino acid formula cost a considerable amount more than extensively hydrolyse formulas and therefore the extensively hydrolysed formula should be trailed first.

- In 2004, the Chief Medical Officer recommended that soya formula should not be used as the first line treatment in the management of infants with CMPA or lactose intolerance under 6 months of age, due to the potential risks of phytoestrogens and possible soya sensitisation. The prevalence of soya allergy in infants with CMPA varies between IgE and non-IgE-mediated disease. Soya formula can be offered as a choice to infants beyond 6 months, who find the hydrolysed formulas unpalatable. Not recommended under 6 months of age.

Indicator for immediate prescription of amino acid based formula and referral to paediatric specialist with experience in managing infants with allergies:

1. **Non IgE CMPA**
    - **a.** Faltering growth with suspected CMPA
    - **b.** Blood in stools
    - **c.** Significant symptoms within the first 12 weeks whilst exclusively breast fed
    - **d.** Severe eczema
2. **IgE CMPA**

Quantities to prescribe

When any infant formula is prescribed the guide below should be used, (for new items, prescribe the required quantity for a two week trial):
For powdered formula:

Age of child	Number of tins for 28 days
Under 6 months	13 x 400g tins or 6 x 900g tins
6-12 months	7-13 x 400g tins or 3-6 x 900g tins
Over 12 months	7 x 400g tins or 3 x 900g tins

Review and discontinuation of formulae on prescription

The need for specialist milk formulas on prescription should be regularly reviewed by either GP, health visitor, paediatrician or dietitian.

All children with milk intolerance should be challenged with milk at or around 12 months, depending on age of diagnosis. Children will generally require 6 months symptom free prior to a milk challenge. Milk challenges should be repeated approximately every 3-6 months. Advice on appropriate foods with which to challenge should be provided by a specialist dietitian. Children should be exposed to low levels of milk initially (e.g. in baked goods, bread/biscuits/cakes) and gradually increased. Cooked milk has a lower allergic risk as the protein is broken down and therefore should be introduced before uncooked milk products. Milk ladder provides a stepwise guidance regarding introduction of milk into diet.

References

NICE 2011 Food Allergy in Children and Young People

Food Hypersensitivity- diagnosing and managing food allergies and intolerances (2009), Skypala I, Venter C. Wiley-Blackwell 978-1-4051-7039-9

Clinical Paediatric Dietetics (2007), Shaw V, Lawson M. Blackwell Publishing 978-14051-3493-4

NHS Cumbria CCG guidelines for prescribers in primary care, Prescribing infant formula in Cows Milk Protein Allergy and Lactose Intolerance. June 2015

County Durham and Darlington NHS Foundation Trust, Guidelines for diagnosing and managing Cows Milk Protein Allergy and Lactose Intolerance. 2015

South Tees Clinical Commisioning Group and Hartlepool and Stockton Clinical Commisioing Group, Sumary of Prescribing for Infant Feeding Problems. October 2015.

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. Yvan Vandenplas, Martin Brueton, Christophe Dupont, David Hill, Erika Isolauri, Sibylle Koletzko, Arnold P Oranje, Annamaria Staiano

Appendix ONE

Extensively Hydrolysed Formulae - for treatment of food hypersensitivity

Brand Name	Marketed as suitable from:	Composition	Designed for:	NHS net ingredient cost	Manufacturer
Milupa Aptamil Pepti 1	Birth	Extensively hydrolysed cow's milk, whey based	Cow's milk protein hypersensitivity (contains lactose)	£9.74/400g	Aptamil/ Milupa (Nutricia)
Milupa Aptamil Pepti 2	from 6 months			£9.29/400g	Aptamil/ Milupa (Nutricia)
Nutramigen 1 with LGG	Birth		Cow's milk hypersensitivity (lactose or protein)	£10.87/400g	Mead Johnson
Nutramigen 2 with LGG	from 6 months			£10.87/400g	Mead Johnson

Extensively Hydrolysed Formulae with MCT* oils - for treatment of food hypersensitivity with other gastrointestinal symptoms

*(medium chain triglycerides)

Brand Name	Suitable from:	Composition	Designed for:	NHS net ingredient cost	Manufacturer
Pepti-Junior	Birth	Extensively hydrolysed cow's milk, whey based with MCT oil	Cow's milk hypersensitivity (lactose or protein), malabsorption	£12.89/450g	Cow & Gate (Nutricia)
Pregestimil Lipil	Birth			£8.91/450g	Mead Johnson

Amino Acid Formulae

Brand Name	Suitable from:	Composition	Designed for:	NHS net ingredient cost	Manufacturer
Neocate LCP	Birth	Amino acids with glucose and MCT oil	Protein/hydrolysate/lactose/ sucrose hypersensitivity, severe malabsorption requiring elemental diet	£28.30/400g	Nutricia/ SHS
Neocate Advance	12 months			£58.50/10 x 100g sachets	Nutricia/ SHS
Nutramigen Puramino	Birth	Amino acids with corn syrup		£26.80/400g	Mead Johnson

Appendix TWO

Recognition of a food allergy (NICE 2011 Food Allergy in Children and Young People)

Consider the possibility of food allergy in children and young people whose symptoms do not respond adequately to treatment for:

- atopic eczema[1]
- gastro-oesophageal reflux disease
- chronic gastrointestinal symptoms, including chronic constipation.

Or has one or more of the signs and symptoms in **Table TWO** (pay particular attention to persistent symptoms that involve different organ systems)

Table TWO. Signs and symptoms of possible food allergy

Note: this list is not exhaustive. The absence of these symptoms does not exclude food allergy

Non-IgE-mediated	**IgE-mediated**
The skin	
Pruritus	Pruritus
Erythema	Erythema
Atopic eczema	Acute urticaria – localised or generalised
	Acute angioedema – most commonly of the lips, face and around the eyes
The gastrointestinal system	
Gastro-oesophageal reflux disease	Angioedema of the lips, tongue and palate
Loose or frequent stools	Oral pruritus
Blood and/or mucus in stools	Nausea
Abdominal pain	Colicky abdominal pain
Infantile colic	Vomiting
Food refusal or aversion	Diarrhoea
Constipation	
Perianal redness	
Pallor and tiredness	
Faltering growth in conjunction with at least one or more gastrointestinal symptoms above (with or without significant atopic eczema)	
The respiratory system (usually in combination with one or more of the above symptoms and signs)	
	Upper respiratory tract symptoms (nasal itching, sneezing, rhinorrhoea or congestion [with or without conjunctivitis])
	Lower respiratory tract symptoms (cough, chest tightness, wheezing or shortness of breath)
Other	
	Signs or symptoms of anaphylaxis or other systemic allergic reactions

[1] For information about treatment for atopic eczema see 'Atopic eczema in children' (NICE clinical guideline 57)