

Paediatric Specialist Group Position Statement Use of Infant Formula based on Soy Protein for Infants

Executive Summary July 2022

There is evidence of potential health risk to infants fed soy infant formula. These guidelines provide a summary of the evidence and guidance on the safe clinical use of soy infant formula for infants under and over the age of 6 months. Health professionals who advise on infant formula should be aware of this information.

Since as early as 2010, the position statement from the Paediatric Specialist Group (PSG) outlined the findings of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) report on phytoestrogens and health (COT 2003), which described the evidence at the time. They reported on the effects of soy infant formula as follows:

“The Working Group considered that the findings from these studies [outlined below] do not provide definitive evidence that phytoestrogens present in soy-based infant formulae can adversely affect the health of infants. However, the findings, together with those from studies on the mechanism of action and biological activity of phytoestrogens reviewed in this Report, provide evidence of potential risks. For this reason, the Working Group expressed concern about the use of soy-based infant formulae. The Working Group noted that the Scientific Advisory Committee on Nutrition (SACN) expressed similar concern when considering evidence presented in this Report. SACN also considered there to be no substantive medical need for, nor health benefit arising from, the use of soy-based infant formulae. However, it was noted that soy-based infant formulae were the only vegan infant formulae option available if babies were not exclusively breast fed. In light of the concerns expressed, the Working Group recommends that the Department of Health review current advice on the use of soy-based infant formulae.”

COT undertook further review of soya phytoestrogens (COT 2013) and their conclusions are included in the most recent publication, ‘Feeding in the First Year of Life’ from SACN (2018):

“There is some uncertainty about the safety of soya-based formula and there is no scientific basis for a change in the current government advice: there is neither substantive medical need for, nor health benefit arising from the use of soya-based infant formula and it should only be used in exceptional circumstances to ensure adequate nutrition.”

“Infant formula (based on either cows’ or goats’ milk) is the only suitable alternative to breast milk for babies who are under 12 months old. The use of soya-based formula should only be

on medical advice and the possible health effects of soya-based formula should be kept under review.”

These recommendations are still relevant today. Neither the American Academy of Pediatrics (Bhatia & Greer 2008) nor the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (Agostoni et al. 2006) have changed their position that there are very few indications for the use of soy infant formula.

Evidence

In the COT report of 2003, two studies raised concern over the possible long-term effects of using soy infant formula in infancy. These relate to a significant increase in prolonged (0.37 days) and painful menstruation in adult women fed soy infant formula as infants (Strom et al. 2001) and increases in the number of Leydig cells in the testes and suppression of the testosterone rise in neonatal marmosets partially fed soy infant formula (Sharpe et al. 2002) compared with cows' milk based infant formula.

The National Toxicity Program Centre for the Evaluation of Risks to Human Reproduction (NTP-CERHR) also suggest that isoflavones are present at similar blood concentrations in infants fed soy infant formula as in rats exhibiting adverse developmental effects (Rozman et al. 2006).

Together with continued concern around the relevance of the aforementioned evidence from human and animal studies, the possibility of adverse effects in soy infant formula cannot be dismissed.

A more recent systemic review with meta-analysis found that soy infant formula can support normal growth and development in full-term infants (Vandenplas et al. 2014). Haemoglobin, serum protein, zinc and calcium concentrations and bone mineral content were found to be similar to those fed breast milk or cow's milk based infant formula, despite the high levels of phytates and aluminium in soy infant formula. However, these were based on a wide range of soy infant formula. Furthermore, nearly all the studies minimally reported on the potential effects of exposure to phytoestrogens on later sexual and reproductive development.

Overall, the PSG believes that this evidence does give rise for concern, and whilst newer evidence is emerging, more extensive studies (particularly more long-term) are needed to clarify the safety of soy infant formula.

Safety of Soy in Infants

As a precautionary measure, the PSG recommend the use of a soy infant formula as first line treatment should be discouraged during the first 6 months of life for the following reasons:

Infants receiving soy infant formula as a sole source of nutrition between the ages of 0-6 months will consume between 6-12 milligrams isoflavones per kilogram body weight per day (Setchell et al 1998). Any potential permanent changes due to phytoestrogens are most likely to occur during this developmental stage of 4-6 months.

Some infants with cow's milk protein allergy (CMPA) may also be sensitised to soy protein, particularly below the age of 6 months (Klemola et al. 2002). The prevalence of concomitant soy protein allergy in infants with CMPA varies between IgE and non-IgE mediated disease (Agostoni et al. 2006). It ranges between 10% and 14% in infants with IgE mediated CMPA (Klemola et al. 2002; Zeiger 1999) but in non-IgE mediated CMPA it is significantly higher (up

to 50%), especially in enterocolitis/enteropathy syndromes (Agostoni et al. 2006). Soy infant formula is not recommended before 6 months of age in infants with food allergy (Turck 2007). This recommendation would clearly extend to soy food products such as desserts and cheeses, as well as soy infant formula.

Furthermore, the European Allergy, Anaphylaxis and Clinical Immunology (EAACI) taskforce suggest against the introduction of soy infant formula in the first 6 months of life to prevent food allergy in infants and young children (Halcken et al. 2020).

Clinical Indications

Breastfeeding should be strongly encouraged as providing the safest and nutritionally adequate form of feeding infants.

The PSG acknowledges that there are clinical indications for feeding soy infant formula in the following groups, as potential risk from soy infant formula is outweighed by clinical concerns:

Infants with CMPA/intolerance who cannot accept extensively hydrolysed or elemental formula: soy infant formula should be avoided in infants under 6 months to avoid sensitisation and exposure to phytoestrogens. In some cases, despite perseverance, an infant may refuse to take extensively hydrolysed or elemental formula, although this is relatively rare as palatability of these has improved in recent years.

Caregivers adopting vegan diets in infants for religious, ethical or other reasons: these caregivers should be strongly encouraged to breastfeed, but if they are unable to breastfeed or choose not to, or require top ups, soy infant formula would be the appropriate choice. This advice would also apply to caregivers following plant-based diets. It is noteworthy that some soy infant formula may not be suitable for vegans (e.g., due to the addition of fish oil, or source of vitamin D) so do check manufacturer guidance.

Galactosaemia: some units consider the lactose content of low lactose formula too high for the treatment of galactosaemia and the use of extensively hydrolysed formula inappropriate. Clearly, for these infants any potential risk of phytoestrogen intake is far outweighed by the risk posed by inappropriate treatment of their galactosaemia.

Any changes to availability of soy infant formula (e.g., prescription only, ACBS approved) must reflect the clinical needs of the above groups.

From the Age of Six Months

From the age of 6 months soy infant formula can be used for the treatment of CMPA/intolerance and lactose intolerance where soy is being considered in the complementary diet. The risks after the age of 6 months are likely to be reduced as the dose of phytoestrogens per kilogram body weight will be lower as the infant begins to take solids. Also, the infant's potentially vulnerable organ systems are likely to have matured by this age, therefore reducing the risk of any long-term harm from soy protein.

Previous research expressed concerns about soy infant formula increasing the risk of developing peanut allergy (Lack et al. 2003). However, a subsequent study concluded that the use of a soy infant formula during the first 2 years of life did not increase the risk for development of peanut-specific IgE antibodies or of clinical peanut allergy at age 4 years (Klemola et al. 2005).

Summary

Breastfeeding should be strongly encouraged as providing the safest and nutritionally adequate form of feeding infants.

Dietitians should discourage the use of soy protein in children with atopy or CMPA in the first 6 months of life to avoid sensitisation to soy protein and exposure to phytoestrogens while organ systems remain at their most vulnerable. This would include soy infant formula and soy products such as desserts and cheeses etc.

When a soy infant formula is used, caregivers should be informed of current findings relating to phytoestrogens and health, as well as the clinical indication for soy infant formula. Any caregiver choosing to refuse soy protein for their infant should be supported in their decision.

Soy infant formula are not recommended for premature infants

More research into the long-term effects of phytoestrogen exposure in infants is needed and into whether any adverse effects are dose related.

This position statement will be reviewed as further evidence becomes available.

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