

What issues should be considered in patients with peanut allergy requiring a medicine containing soya?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals
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Background

As peanut and soya belong to the same plant family (legumes), concern has been raised that patients allergic to peanuts might also be allergic to soya. There is however no consistent published advice on the risk of cross-sensitivity.

Soya may be included as an excipient in medicines. However, there is inconsistency in the prescribing information in the Summaries of Product Characteristics (SPCs) of soya-containing medicines regarding whether or not they are contra-indicated in individuals who are hypersensitive to peanuts.

For information about arachis oil in medicines, please see UKMi Medicines Q&A: "[Arachis oil in medicines – what are the risks of developing peanut allergy?](#)"

Answer

Peanut and soya allergy

Peanuts are not actually nuts, but are members of the legume family, which also includes soya, peas, beans and lentils (1).

Some peanut allergic individuals are also allergic to other legumes, including soya, and fatalities have been reported in some patients with a known severe food allergy to peanut after ingesting soya-containing foods (2,3). There is an expectation that similar proteins across the legume family will cause reactions in some individuals (1). However, in practice, cross-reactivity appears to be rare (2,4).

Soybean oil is claimed to be the world's most widely used edible oil, with almost all margarines containing it (5). Soy or derivatives of soy are found in some infant formulas, and in many commercially available processed foods (4,6,7). It is also a common ingredient in Asian cuisine. Therefore, many patients allergic to peanuts will have inadvertently ingested soy or soy oil in these foods without realising it.

As with most food allergies peanut allergy is commonly immunoglobulin E (IgE)-mediated (5). There is limited information available regarding cross-reactivity between peanuts and soya. Some articles suggest that whilst there is frequent cross-reactivity to foods within a botanical family e.g. legumes (as assessed by blood tests [specific IgE] or skin prick tests), an actual clinical (allergic) cross-reaction is much less common (1,8,9). For this reason, people who are allergic to peanuts do not usually need to avoid dietary consumption of soya or other foods in the legume family, although if there is clinical concern, specialist advice and/or referral for allergy testing is recommended before introducing other potentially allergenic foods, particularly for higher risk individuals with a history of anaphylaxis or with a personal or family history of multiple allergies (4,6,10-13).

A study of double-blind placebo-controlled food challenges (DBPCFC) carried out in 113 children and young adults with severe atopic dermatitis showed that 19% reacted to peanut and 5% to soya (8). Whilst many patients had positive skin prick test reactions to several members of a botanical family e.g. legumes, only one patient reacted to two members of the bean family following DBPCFC. The authors suggest that

clinical hypersensitivity tends to be specific to individual food antigens, whereas skin test sensitivity reflects some common antigens among members of a particular botanical family. No patient sensitive to peanut reacted to any other member of the legume family tested.

A study of DBPCFC in 32 children with peanut allergy found that while 17 had a positive skin test to soya, only 1 patient with a positive double-blind oral peanut challenge also had a positive double-blind oral soya challenge (9). These results are similar to those reported elsewhere, where only 3 of 165 children and young adults reacted to both peanut and another (unspecified) legume at oral food challenge (details of skin sensitisation and cross-reactivity between peanuts and soya were not reported) (14). Bernhisel-Broadbent and Sampson performed DBPCFC in 69 children and young adults with positive skin tests to legumes, of whom 41 had clinical reactions to legumes (1). Two of these patients had clinically relevant food hypersensitivity to both peanut and soya. The authors concluded that elimination of all legumes in individuals with clinical reactions to one legume was unwarranted unless hypersensitivity to each antigen is individually confirmed by DBPCFC (1). In another DBPCFC study in 68 children in the US aged 8 to 16 years with a history of anaphylaxis to peanut, 3% of the cohort with challenge-proven peanut allergy (n=64) were found to have concomitant soya allergy (7).

Guidelines

British Society for Allergy and Clinical Immunology guidelines on diagnosis and management of peanut and tree nut allergy caution that “peanut-allergic individuals may be sensitised to legumes (soya, pea and chickpea)” but note that the rate of allergy is low in the UK (15).

In the United States, National Institute for Allergy and Infectious Diseases guidelines for food allergy recommend that, while the specific allergen or allergens should be avoided in patients with documented IgE-mediated food allergy, health care professionals should decide with their patients whether certain cross-reactive foods should also be avoided (10). This guidance takes into account the variability in rates of clinically relevant cross-reactivity to related foods in patients with known allergy to a food, and suggests that health care professionals may need to individualise additional testing and patient instructions depending on the foods involved. A summary table provides estimates of rates of clinically relevant cross reactivity of certain foods, with peanut vs soya at 3-5%, but notes the limited study data available.

Manufacturers' information

There may be inconsistency in the cautionary and contraindications information contained in the Summaries of Product Characteristics (SmPCs) of soya-containing medicines. Although the majority of preparations containing soya are specifically contraindicated in individuals hypersensitive to soya or peanuts, this may not be the case for all products (16). There may also be inconsistency in identifying soya oil as an excipient in product SPCs, with other terms such as “edible fats” or “vegetable oils” sometimes used.

Current European guidelines for labelling of excipients in medicinal products state that products that contain any amount of soya oil or hydrogenated soya oil, should provide the following information in the package leaflet “<Medicinal product> contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product”, and a contraindication should be included in the SmPC (17).

Food labelling regulations, however, vary slightly. Although there is a direction that any presence of “soybeans and products thereof” (including soy lecithin) must be declared as an allergen on the packaging, there is an exemption for “fully refined soybean oil” (the type of oil usually present in medicines)-(7,18,19). This is because the European Food Safety Agency has assessed these products as not possessing allergenic risk since the allergen/protein has been removed by the refining process. The manufacturer's contraindications and cautions should always be borne in mind when choosing a product. Ideally patients with peanut allergy should avoid products containing soya ingredients. Soya-free

alternatives can be identified by checking the medicine's ingredients (excipients) using the individual SmPC.

There may be clinical circumstances when use of a particular medication containing soya is necessary (20). In this case, a risk/benefit judgement will be required. Although outside the scope of this Q&A, the medical literature reports on such cases, particularly for use of the general anaesthetic, propofol, and for isotretinoin and alitretinoin, oral retinoids used in dermatology, all of which contain soybean oil and are therefore contraindicated in people who are hypersensitive to peanut (and soya) (21-23). Data are limited to small retrospective studies or case reports, but for the most part use of the soya-containing medicine was successful (24-29). Strategies described in these studies to minimise risk include prior allergy testing or provocation with small doses followed by close monitoring in a hospital setting with facilities for managing anaphylaxis. Some hospitals may have in-house protocols for treating patients with peanut allergy with soya-containing medicines (27,28,30).

Summary

- ♦ As peanut and soya belong to the same plant family (legumes), there is concern that patients allergic to peanuts might also be allergic to soya. There is no consistent published advice on the risk of cross-sensitivity, and further studies are required to quantify the risk, but it appears to be rare.
- ♦ Some articles suggest that whilst there is frequent cross-reactivity to foods within a botanical family as assessed by blood tests or skin prick tests, an actual clinical (allergic) cross-reaction is much less common. Demonstration of clinical reactivity may be required by food challenge, as skin allergy tests may have a low predictive value.
- ♦ People who are allergic to peanuts do not usually need to avoid soya in their diet. However, if there is any clinical concern then patients should be referred for specialist investigations, particularly if they are higher risk.
- ♦ European medicines labelling guidelines recommend that where products contain soya oil (and hydrogenated soya oil), this should be declared, with a warning in the package leaflet for patients who are allergic to soya or peanuts not to use the product, and a contraindication included in the Summary of Product Characteristics (SmPC). Food labelling regulations also require declaration of any soy or soy products, but offer exemption for "fully refined" soybean oil, with regulators assessing that the refining process will have removed any allergenic potential.
- ♦ Whilst the majority of medicines containing soya are specifically contraindicated in individuals hypersensitive to soya or peanuts, there may be inconsistency. Individual SmPCs should be checked before prescribing to be aware of any contraindications or cautions that may apply to the use of a specific product.
- ♦ To identify a soya free medicine, the ingredients can be checked using the individual SmPC. There may be clinical circumstances when use of a product containing soya ingredients may be necessary in a patient with peanut allergy. In this case, a risk/benefit judgement will be required and strategies to minimise risk may be employed. There are reports of this scenario in the medical literature, in particular for the general anaesthetic, propofol and for retinoid medicines used in dermatology, e.g. isotretinoin

Limitations

- ♦ There is limited published information available regarding cross-reactivity between peanuts and soya and very few recent published studies are available.
- ♦ Published studies investigating cross-reactivity to peanuts and soya have included small numbers of patients and have only been conducted in children and young adults.
- ♦ Discussion of the risk of cross-reactivity between peanuts and tree nuts (such as hazelnuts or Brazil nuts) or other legumes (e.g. lentils, chick peas) is beyond the scope of this document.

- ♦ Individual Summary of Product Characteristics and Patient Information Leaflets should be checked before prescribing as formulations may change.
- ♦ Herbal or complementary medicines have not been considered in this Medicines Q&A.

Acknowledgement

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Search strategy

- Embase (via OVID):

1. exp peanut/ OR exp peanut allergy/
 2. exp soybean/ OR exp soybean oil/
 3. EMBASE; exp cross allergy/ OR exp allergy/ OR exp peanut allergy/ OR exp food allergy/
 4. 1 AND 2 AND 3.
- Medline search (via OVID):
 1. exp Arachis/
 2. exp Soybeans/
 3. exp Hypersensitivity/
 4. exp Cross Reactions/
 5. 3 AND 4
 6. 1 AND 2 AND 5
 - NICE Evidence <https://www.evidence.nhs.uk/>
 - Cochrane Library <https://www.cochranelibrary.com/search>
 - British Society for Immunology www.immunology.org
 - British Society for Allergy and Clinical Immunology www.bsaci.org
 - American College of Allergy, Asthma and Immunology <https://acaai.org/>
 - Food Standards Agency <https://www.food.gov.uk/>
 - General internet search (Google)
 - Uptodate website www.uptodate.com
 - European Medicines Agency <http://www.ema.europa.eu/ema>
 - Medicines and Healthcare products Regulatory Agency <http://www.mhra.gov.uk/index.htm>
 - Clinical experts: consultant immunologist, consultant dermatologist and allergy multi-disciplinary team at University Hospital Southampton NHS Foundation Trust.