Handling questions about excipients

Introduction

Pharmaceutical excipients are constituents of a medicine used not for their direct therapeutic action but to aid the manufacturing process, such as to enhance stability or bioavailability. Ideally excipients have no pharmacological action, are non-toxic and do not interact chemically or physically with active ingredients or other excipients, but this is rarely the case. (1)

Patients may want or need to avoid certain pharmaceutical excipient(s) for a number of reasons. Medicines free from specific pharmaceutical excipient(s) may be requested for particular patient groups (e.g. neonates), patients with a severe allergy or with particular cultural or religious beliefs. This document is intended to support that decision.

Certain excipients may be of vegetable and animal origin. If this is important, then you should check the origin of the excipient in that particular product. If asked about excipients for vegans there is a useful UKMI Q&A on what you should consider. (2)

How to check for the presence or absence of the substance in product information

- You need the product brand name or generics manufacturer because the information is brand specific and can also be batch specific.
- For some substances, the immediate/outer packaging of the product will state if the substance is present.
- All excipients are listed in the Patient Information Leaflet (PIL), and if the pack leaflet is available it is the preferred source of information. This is because there can sometimes be a short time lapse between batch formulation changes and online PIL and SmPC updates. (3)
- If you do not have the pack leaflet, the online PIL and SmPC will list the excipients.
- If you have been asked which brand/product should be prescribed, consult the electronic Medicines Compendium. The advanced search function (https://www.medicines.org.uk/emc/advanced-search) allows you to search for products which do *not* contain a substance. Check the excipient list in each of those SmPC individually before informing your enquirer.
- If considered vital to avoid all exposure to a given excipient, it is advisable wherever possible, to contact the manufacturer to check product contents.
- If you are unable to contact the manufacturer, a judgement is to be made, based on the available information as to the need for the medicines and the likelihood of, and the risk associated with, the presence of that excipient.

Excipients in the labelling and package leaflet of medicinal products for human use

All excipients must be declared on the outer packaging or, where there is no outer packaging, on the immediate packaging of the medicinal product and the SmPC of injectable, topical or eye preparations. (4)

Pharmaceutical Excipients

The EMA has issued guidance with a list of excipients which must feature in the leaflet packaging of medicinal products and the way in which these excipients must be indicated. These excipients are those known to have a recognised action. (5)

Some excipients require additional warnings when any of the substance is present at all; others only require a warning above a certain threshold. The warnings necessary may also depend on the route of administration of the product. (4)

For example all medicinal products containing any arachis oil must include the following warning statement in the SmPC and patient information leaflet (PIL),

'<Medicinal product> contains arachis oil (peanut oil). If you are allergic to peanut or soya, do not use this medicinal product.'

The following excipients carry a warning statement if present in any amount (i.e. they have a zero threshold). Where the zero threshold applies only to certain routes of administration, this is stated. Other routes may have higher threshold amounts.

Aprotinin (topicals only)	Lactitol (E996) (oral) (topical)
Arachis oil (peanut oil)	Lactose (oral)
Aspartame (E951) (oral only)	Lanolin (wool fat)
Azo colouring agents (oral only)	Latex (all)
Balsam of Peru (topical only)	Macrogolglycerol ricinoleate and macrogolglycerol hydroxystearate (oral, parenteral, topical)
Benzalkonium Chloride (all)	Maltitol (E965) (oral)
Benzoic acid (E210) and benzoates (all)	Metabisulphites (oral, parenteral, inhalation)
Benzyl alcohol (all)	Organic mercury compounds (ocular, topical, parenteral)
Bergamot Oil (containing bergaptan) (topical only)	Parahydroxybenzoates and their esters (oral, ocular, topical, parenteral, inhalation)
Bronopol (topical only)	Phenylalanine
Butylated hydroxyanisole (E320) (topical only)	Phosphate buffers (ocular)
Butylated hydroxytoluene (E321) (topical only)	Potassium (parenteral)
Cetosteryl alcohol including cetyl alcohol (topicals only)	Sesame oil
Chlorocresol (topical, parenteral)	Sodium
Dimethyl sulphoxide (topical)	Sodium laurilsulfate (topical)
Ethanol (oral, parenteral, inhalation, cutaneous)	Sorbic acid (E200) and salts (topical)
Formaldehyde (topical, oral)	Sorbitol (E420) (oral, parenteral)
Fragrances containing allergens (topical)*	Soya oil, hydrogenated soya oil
Fructose (oral, parenteral)	Stearyl alcohol (topical)
Galactose (oral, parenteral)	Sucrose (oral)
Glucose (oral)	Sulphites (oral, parenteral, inhalation)
Heparin (parenteral)	Wheat starch (oral)

Invert sugar (oral)	Wool fat (lanolin) (topical)
Isomalt (E953) (oral)	

*Any known allergenic components of fragrances or flavourings should be listed in the SmPC.

Other excipients are required to carry a warning only if present above a certain threshold:

Boric acid	Mannitol
Cyclodextrins	Potassium (oral only)
Fructose (Oral, parenteral (other than IV))	Propylene glycol (E1520) and esters of propylene glycol
Glucose (parenteral)	Xylitol (E967)
Glycerol	

Impurities and Residues from the Manufacturing Process

Residues of substances arising from the manufacturing process, impurities, residual solvents, degradation products etc. are not classed as excipients. (6) The guidance on excipients in pharmaceuticals therefore does not apply to them and they are not required to be listed in product information.

Vaccines are a special case. Separate guidance states that “residues of clinical relevance” (e.g. traces of antibiotics, host cell proteins, or some chemicals) must be mentioned in the SmPC.

A manufacturer may not guarantee that a product has not come into contact with a substance during the manufacturing process, even if the product does not actually contain the substance (such as an allergen or latex). Advice may therefore rely on balancing the potential risk to the patient against the benefit or need.

References

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