Pharmacopoeias. In *US*.
USP 31 (Sodium Monofluorophosphate). A white to slightly grey, odourless powder. Freely soluble in water. pH of a 2% solution in water is between 6.5 and 8.0.

Profile
Sodium monofluorophosphate is used as a source of fluoride (see Sodium Fluoride, p.1962) in toothpastes for the prevention of dental caries. It may also be given by mouth in the management of osteoporosis.

In the UK, the maximum permitted fluoride level in toothpastes is 1.14% of sodium monofluorophosphate (0.15% or 1500 ppm of fluoride). Formulations for children under 7 years of age typically contain sodium monofluorophosphate 0.38% (500 ppm fluoride); higher concentrations may be used, but the amount applied should be supervised to avoid excessive use or ingestion.

Other monofluorophosphate salts permitted for use in oral hygiene products and dentifrices include ammonium monofluorophosphate, calcium monofluorophosphate, and potassium monofluorophosphate. Glutamine monofluorophosphate has been used for osteoporosis.

Osteoporosis. For reference to the use of fluorides, including sodium monofluorophosphate, in the treatment of osteoporosis, see under Uses of Sodium Fluoride, p.1964.

Preparations
Proprietary Preparations (details are given in Part 3)

Arg.: Osteomar†; ***Austral.:*** Fluorocare; ***Austria:*** Osteopro; ***Braz.:*** Emoform AP; Malvatricin Antitartaro; Unique Plus; ***Chile:*** Fluocaril Bi-Fluore; Gengisyl; Oralfresh; ***Cz.:*** Difluena†; ***Ger.:*** Mono-Tridin; ***Ital.:*** Clinomyn; Isifluor; Neo Emoform†; Neo Fluostomygen; Platinum.

Multi-ingredient: ***Arg.:*** Desensyl; Emoform Total; Fluocalcic†; Fluordent PX; Hexiben; Hexiben Plus†; Negaporosis; Odol Med Antiplaca†; Sensodyne-F; Squam; ***Austria:*** Fluocalcic; ***Belg.:*** Fluocalcic†; Fluocaril; ***Braz.:*** Emoform AT; Fluomint; Malvatricin Antiplaca; Malvatricin Branqueador; Malvatricin Dentes Sensiveis; Malvatricin Natural; Malvatricin Natural Organic; Malvatricin Natural Soft; Malvatricin Plus; Sensodyne-F; ***Canad.:*** Viadent†; ***Chile:*** Caristop; Gingilacer†; Sensilacer†; Tridin†; ***Cz.:*** Fluocalcic†; Fluocaril Bi-Fluore Vitamin E†; Fluocaril Bi-Fluore†; Tridin; ***Fr.:*** Emoform Dents Sensibles; Fluocaril Bi-Fluore; Fluocaril blancheur; Fluocaril Junior and Fluocaril Kids; Sanogyl Fluo†; Sanogyl Junior†; Sanogyl†; ***Ger.:*** Calcivit F†; Fluoril; Tridin; Tridin Forte; ***Hong Kong:*** Tridin; ***Hung.:*** Tridin; ***Ital.:*** Aqua Emoform†; Biogreen; Broxo al Fluoro; Broxodin†; Calcitridin†; Dentosan Carie & Alito†; Dentosan Junior; Emoform-Tat†; Eudent con Glysan†; Fluocaril Bi-Fluore; Formedico; Neo-Stomygen; Orosanyl†; Periogard Plus; Stomygen; Tridin; ***Mex.:*** Dentsiblen; Fluoxytil; Periodentyl; ***Pol.:*** Fluoro-zel; ***Port.:*** Fluocaril Bi-Fluore; ***Switz.:*** Emoform-F au fluor; Fluo-calc†; Fluocaril Bi-Fluore†; ***Turk.:*** Sensodyne-F; ***USA:*** Monocal; Optimoist; Sensodyne-F; ***Venez.:*** Sensident†; Topdent†.

Sodium Silicofluoride
Fluosilicato sódico; Sodium Fluorosilicate; Sodium Fluosilicate; Sodium Hexafluorosilicate.

Na_2SiF_6 = 188.1.
CAS — 16893-85-9.

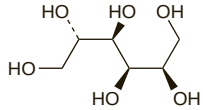
Profile
Sodium silicofluoride is used as a source of fluoride (see Sodium Fluoride, p.1962) for the fluoridation of drinking water. It has also been considered for inclusion in oral hygiene products.

Other silicofluoride (fluorosilicate) salts permitted for use in oral hygiene products include ammonium silicofluoride, magnesium silicofluoride, and potassium silicofluoride.

Sodium silicofluoride has also been used in insecticides.

Sorbitol
E420; D-Sorbitol; Sorbitoli; Sorbitolis; Sorbitolum; Szorbit. D-Glucitol.

$C_6H_{14}O_6$ = 182.2.
CAS — 50-70-4.
ATC — A06AD18; A06AG07; B05CX02; V04CC01.
ATC Vet — QA06AD18; QA06AG07; QB05CX02; QV04CC01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *Viet.* Also in *USNF*.
US includes only Sorbitol Solution.
Ph. Eur. 6.2 (Sorbitol). A white or almost white crystalline powder. It exhibits polymorphism. Very soluble in water; practically insoluble in alcohol.
USNF 26 (Sorbitol). White, odourless, hygroscopic powder, granules, or crystalline masses having a sweet taste with a cold sensation. Soluble 1 in 0.45 of water; sparingly soluble in alcohol; practically insoluble in solvent ether. pH of a 10% w/w solution in water is between 3.5 and 7.0.

Incompatibility. For reference to the incompatibility of sorbitol with hydroxybenzoates, see p.1649.

Adverse Effects and Precautions
As for Fructose, p.1945.

Effects on electrolyte balance. Sorbitol is used as a vehicle in some proprietary preparations of activated charcoal intended to reduce drug absorption after poisoning; the sorbitol increases the palatability of the preparation and also produces an osmotic diarrhoea that facilitates elimination of the activated charcoal and adsorbed drug. Repeated doses of such preparations are often advocated but there have been reports[1-3] of severe sorbitol-induced hypernatraemia in adults and children. In all cases, charcoal in a 70% sorbitol suspension had been given. It has been recommended that fluid and electrolyte balance be monitored closely, and that preparations with lower concentrations of sorbitol be used if possible.[2,3] For debate about such multiple dose therapy see Poisoning, under Activated Charcoal, p.1436.

1. Gazda-Smith E, Synhavsky A. Hypernatraemia following treatment of theophylline toxicity with activated charcoal and sorbitol. *Arch Intern Med* 1990; **150:** 689 and 692.
2. Allerton JP, Strom JA. Hypernatremia due to repeated doses of charcoal-sorbitol. *Am J Kidney Dis* 1991; **17:** 581–4.
3. Farley TA. Severe hypernatremic dehydration after use of an activated charcoal-sorbitol suspension. *J Pediatr* 1986; **109:** 719–22.

Effects on the gastrointestinal tract. Sorbitol is often used as a sweetener in sugar-free preparations and the risk of sorbitol-induced diarrhoea associated with such products has been highlighted.[1-4] Chronic sorbitol-induced diarrhoea with associated pneumatosis intestinalis has been reported in a child given 21.7 g sorbitol daily in liquid medications.[5] Colonic and upper gastrointestinal necrosis, including some fatalities, have been reported after use of sodium polystyrene sulfonate in sorbitol, and may have been associated with the sorbitol component, see p.1465.

It has also been suggested that sorbitol contributed to the morbidity in a patient who developed septicaemia as a complication of intestinal pseudo-obstruction, after the use of charcoal with sorbitol to treat self-poisoning with theophylline.[6] It was suggested that gaseous distension after bacterial metabolism of sorbitol had rendered the bowel wall ischaemic, facilitating passage of bacteria or of endotoxin into the systemic circulation.

1. Brown AM, Masson E. 'Hidden' sorbitol in proprietary medicines - a cause for concern? *Pharm J* 1990; **245:** 211.
2. Edes TE, *et al*. Diarrhea in tube-fed patients: feeding formula not necessarily the cause. *Am J Med* 1990; **88:** 91–3.
3. Johnston KR, *et al*. Gastrointestinal effects of sorbitol as an additive in liquid medications. *Am J Med* 1994; **97:** 185–91.
4. Bauditz J, *et al*. Severe weight loss caused by chewing gum. *BMJ* 2008; **336:** 96–7.
5. Duncan B, *et al*. Medication-induced pneumatosis intestinalis. *Pediatrics* 1997; **99:** 633–6.
6. Longdon P, Henderson A. Intestinal pseudo-obstruction following the use of enteral charcoal and sorbitol and mechanical ventilation with papaveretum sedation for theophylline poisoning. *Drug Safety* 1992; **7:** 74–7.

Pharmacokinetics
Sorbitol is poorly absorbed from the gastrointestinal tract after oral or rectal use. It is metabolised mainly in the liver, to fructose (see p.1945), a reaction catalysed by the enzyme sorbitol dehydrogenase. Some sorbitol may be converted directly to glucose by the enzyme aldose reductase.

Uses and Administration
Sorbitol is a polyhydric sugar alcohol (polyol) with half the sweetening power of sucrose. It occurs naturally in many fruits and vegetables and is prepared commercially by the reduction of glucose.

It has been given as a 30% solution as an alternative to glucose in parenteral nutrition (p.1923) but its use is not recommended because of the risk of lactic acidosis.

Sorbitol may be given orally or rectally as an osmotic laxative in the management of constipation (p.1693); doses of 20 to 50 g have been suggested.

Solutions containing about 3% of sorbitol are used as irrigating fluids in transurethral surgical procedures.

Sorbitol was formerly given intravenously as a 50% solution as an osmotic diuretic.

Sorbitol also acts as a bulk sweetening agent. It is used in limited quantities as a sweetener in energy-reduced diabetic food products. It is also used as an alternative to sucrose in many sugar-free oral liquid preparations and in sugar-free foods as it is less likely to cause dental caries.

Sorbitol also has humectant and stabilising properties and is used in various pharmaceutical and cosmetic products including toothpaste.

Preparations
Ph. Eur.: Sorbitol, Liquid (Crystallising); Sorbitol, Liquid (Non-crystallising); Sorbitol, Liquid, Partially Dehydrated;
USNF 26: Noncrystallizing Sorbitol Solution;
USP 31: Sorbitol Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Progras†; ***Austral.:*** Sorbilax; ***Braz.:*** Minilax; ***Cz.:*** Ardeanutrisol SO†; ***Hung.:*** Szorbit†; ***Swed.:*** Cystosol†; Resulax.

Multi-ingredient: ***Arg.:*** Humectante Bucal; Micronema; ***Austral.:*** Aquae; Carbosorb S; Fleet Micro-Enema; Medevac†; Microlax; ***Austria:*** Glandosane; Lemazol; Microklist; Resectal; Trommgallol; Yal; ***Belg.:*** Microlax; Spagulax Sorbitol; ***Braz.:*** Anekron; Bilifluxt†; Colachofra; Hepalin; Hepatobe†; Hepatox; Hormo Hepatico†; ***Canad.:*** Charac Tol; Charcodote; Microlax; Salivart; ***Chile:*** Salivart†; Secand; Tabletas Phillips; ***Cz.:*** Yal; ***Denm.:*** Klyx; ***Fin.:*** Klyx; Microlax; Somanol + Ethanol; ***Fr.:*** Apilaxe†; Artisial; Exova†; Hepacholine†; Hepagrume; Hepargitol; Microlax; Nivabetol; Ornitaine; Parapsyllium; Schoum; Spagulax au Sorbitol; SST; ***Ger.:*** Flacar; Freka-Drainjet Purisole; Glandosane; Klysma Sorbit; Microklist; Tutofusin S†; Yal; ***Hong Kong:*** Aquae; Glandosane; Microlax; Salivart; ***Hung.:*** Balansol; Yal†; ***India:*** Alkasol-P; Livocip; Mecolin; Sorbiline; Sorliv; ***Indon.:*** Laxarec; Microlax; ***Israel:*** Charcodote; Spray Mint; ***Ital.:*** Citroepatina; Macrolax; Magisbile†; Novilax; Sorbiclis; ***Malaysia:*** Microlax†; ***Mex.:*** Clyss-Go; ***Neth.:*** Klyx; Microlax; ***Norw.:*** Klyx; Microlax; ***NZ:*** Carbosorb S†; Carbosorb XS; Medevac†; Microlax; ***Pol.:*** Purisole SM; Rektiolax; ***Port.:*** Clyss-Go; Glandosane; Purisole; ***Rus.:*** Microlax (Микролакс); ***S.Afr.:*** Agofell; Microlax†; ***Spain:*** Sugarbil; Vitaphakol; ***Swed.:*** Klyx; Microlax; Vi-Siblin S; ***Switz.:*** Agarol Soft; Citral†; Glandosane; Microklist; Pursana; Yal; ***Thai.:*** Glandosane†; ***Turk.:*** Charflo Sorbitol; Kansilak; Libalaks; Sabalax; ***UK:*** Glandosane; Luborant; Relaxit; Saliva Natura; SST; ***USA:*** Actidose with Sorbitol; Moi-Stir; Numoisyn; Plax; Salivart; ***Venez.:*** Clys-Go†.

Soya Bean
Habas de soja; Soja Bean; Soyabean; Soybean.

Description. Soya bean is the seed of the soya plant *Glycine max* (*G. hispida*; *G. soja* (L.) Merr.). It is a source of soya oil and soya protein.*G.soja* Siebold & Zucc. is wild soybean.

Soya Oil
Aceite de soja; Soiae Oleum; Soijaöljy; Soja Bean Oil; Soja, huile de; Sojae oleum; Sojaolja; Sójový olej; Sojų aliejus; Soya Yağı; Soyabean Oil; Soya-bean Oil; Soybean Oil; Szójababolaj.

Pharmacopoeias. In *Chin.*, *Jpn*, and *US*.
Eur. (see p.vii) includes both hydrogenated and refined oils. *Ger.* also includes a partially hydrogenated oil. *USNF* includes the hydrogenated oil.
Ph. Eur. 6.2 (Soya-bean Oil, Refined; Soiae Oleum Raffinatum). It is the fatty oil obtained from seeds of *Glycine soja* and *G. max* (*G. hispida*) by extraction and subsequent refining. It may contain a suitable antoxidant and is a clear, pale yellow liquid. Practically insoluble in alcohol; miscible with petroleum spirit. Store in well-filled containers at a temperature not exceeding 25°. Protect from light.
The BP 2008 directs that when Soya Oil, Soyabean Oil, or Soyabean Oil is demanded, Refined Soya Oil shall be supplied.
Ph. Eur. 6.2 (Soya-bean Oil, Hydrogenated; Soiae Oleum Hydrogenatum). It is obtained by refining, bleaching, hydrogenation, and deodorisation of soya oil. It consists mainly of triglycerides of palmitic and stearic acids and is a white or almost white mass or powder which melts to a clear, pale yellow liquid when heated. Practically insoluble in water; very slightly soluble in alcohol; freely soluble in dichloromethane, in petroleum spirit after heating, and in toluene. Protect from light.
USP 31: (Soybean Oil). The refined fixed oil obtained from the seeds of the soya plant *Glycine max* (Fabaceae). It may contain suitable antoxidants. A clear, pale yellow, oily liquid having a characteristic odour. Insoluble in water; miscible with chloroform and with ether. Store in airtight containers at a temperature not exceeding 40°. Protect from light.
USNF 26 (Hydrogenated Soybean Oil). The product obtained by refining, bleaching, hydrogenation, and deodorisation of oil obtained from seeds of the soya plant, *Glycine max* (Fabaceae). It consists mainly of triglycerides of palmitic and stearic acids. A white mass or powder that melts to a clear, pale yellow liquid when heated. M.p. between 66° and 72°. Practically insoluble in water; very slightly soluble in alcohol; freely soluble in dichloromethane, in petroleum spirit after heating, and in toluene. Store in airtight containers. Protect from light.

Incompatibility. For mention of the compatibility and stability of solutions and emulsions for parenteral nutrition see under Enteral and Parenteral Nutrition, p.1924.

Adverse Effects

Hypersensitivity reactions including fever and chills have been reported after the infusion of soya oil emulsion although they are considered to be fairly rare. Other rare immediate reactions include dyspnoea, cyanosis, hyperlipidaemia, hypercoagulability, nausea, vomiting, headache, and chest and back pain. Delayed reactions include hepatomegaly, splenomegaly, jaundice due to cholestasis, thrombocytopenia, leucopenia, and transient increases in liver function tests.

Prolonged or too rapid infusion of soya oil emulsion or its use in patients with impaired fat metabolism has been associated with the 'overload syndrome'. This is manifested by anaemia, leucocytopenia, thrombocytopenia, and impaired coagulation, hepatosplenomegaly, hyperlipidaemia, fever, focal seizures, shock, and coma. Metabolic acidosis has been associated with severe overdosage especially if carbohydrates are not also given. Pigmentation of tissues in the reticuloendothelial system after prolonged therapy with lipid emulsion infusions has also been reported.

Soya protein-based infant feeds can be antigenic and cause gastrointestinal adverse effects in sensitive individuals.

Bacteraemia. A strong association has been found between giving lipids through peripheral venous catheters made of Teflon and development of coagulase-negative staphylococcal bacteraemia in neonates.[1] It was suggested that investigation of catheters made of other materials, or other delivery systems, might reduce the opportunity for coagulase-negative staphylococci to adhere and come into contact with nutrient-rich growth media in the form of lipid emulsions. Others also took the view that this work should not lead to the abandonment of parenteral lipids in premature infants.[2]

1. Freeman J, *et al.* Association of intravenous lipid emulsion and coagulase-negative staphylococcal bacteremia in neonatal intensive care units. *N Engl J Med* 1990; **323:** 301–8.
2. Klein JO. From harmless commensal to invasive pathogen: coagulase-negative staphylococci. *N Engl J Med* 1990; **323:** 339–40.

Effects on the cardiovascular system. Sinus bradycardia has been reported in a patient receiving total parenteral nutrition that included soya oil-based emulsion via a central line.[1] The authors suggested that it might be wise to give fat emulsion only through a peripheral vein. However, sinus bradycardia has been reported after a safflower oil-based emulsion given via a peripheral vein as part of a TPN regimen.[2]

1. Sternberg A, *et al.* Intralipid-induced transient sinus bradycardia. *N Engl J Med* 1981; **304:** 422–3.
2. Traub SL, *et al.* Sinus bradycardia associated with peripheral lipids and total parenteral nutrition. *J Parenter Enteral Nutr* 1985; **9:** 358–60.

Effects on the endocrine system. Soya bean is a rich source of phytoestrogens including isoflavones, and it has been found that infants fed soya-based formula have high serum concentrations of these substances,[1] which has brought the safety of soya-based formulas into question. *Animal* and *in vitro* data suggest that isoflavones such as genistein have pharmacological effects on growth and development.[2] However, genistein and daidzein are less potent than endogenous oestrogens and have less binding affinity to oestrogen receptors.[3] It is not known to what extent infants are able to metabolise and deconjugate soya isoflavones.[4] A small retrospective study[5] observed no oestrogenic effects in children fed soya protein formula for at least 6 months. A larger retrospective cohort study[6] in adults observed no statistically significant differences between those who had been fed soya formula and those fed cow's milk formula as infants.

As yet, there is insufficient evidence of harm from soya-based formulas,[7] although further studies are deemed necessary to assess long-term effects.[2,4] The American Academy of Pediatrics[8] considers soya protein-based formulas to be safe and effective in healthy term infants, while providing no advantage over cow's milk protein-based formulas. However, soya-based formulas are not recommended for use in low birth-weight preterm infants because of concerns about poorer growth rates compared with infants given formulas based on cow's milk protein.

Before their supplementation with iodine, there had been reports of hypothyroidism associated with soya formula feeds. Abnormal thyroid function tests have since been reported in infants fed with soya formulas, and a retrospective analysis of infants with congenital hypothyroidism found those fed with soya took longer for their thyroid stimulating hormone levels to normalise.[9]

1. Setchell KDR, *et al.* Exposure of infants to phyto-oestrogens from soy-based infant formula. *Lancet* 1997; **350:** 23–7.
2. Chen A, Rogan WJ. Isoflavones in soy infant formula: a review of evidence for endocrine and other activity in infants. *Annu Rev Nutr* 2004; **24:** 33–54.
3. Miniello VL, *et al.* Soy-based formulas and phyto-oestrogens: a safety profile. *Acta Paediatr Suppl* 2003; **91:** 93–100.
4. Mendez MA, *et al.* Soy-based formulae and infant growth and development: a review. *J Nutr* 2002; **132:** 2127–30.
5. Giampietro PG, *et al.* Soy protein formulas in children; no hormonal effects in long-term feeding. *J Pediatr Endocrinol Metab* 2004; **17:** 191–6.
6. Strom BL, *et al.* Exposure to soy-based formula in infancy and endocrinological and reproductive outcomes in young adulthood. *JAMA* 2001; **286:** 807–14.
7. Tuohy PG. Soy infant formula and phytoestrogens. *J Paediatr Child Health* 2003; **39:** 401–5.
8. American Academy of Pediatrics Committee on Nutrition. Soy protein-based formulas: recommendations for use in infant feeding. *Pediatrics* 1998; **101:** 148–53. Also available at: http://www.pediatrics.org/cgi/content/full/101/1/148 (accessed 08/11/05)
9. Conrad SC, *et al.* Soy formula complicates management of congenital hypothyroidism. *Arch Dis Child* 2004; **89:** 37–40.

Effects on the nervous system. CNS disorders in 2 patients given infusions of fractionated soya emulsion included convulsions and coma; cortical blindness developed in one young woman.[1] A similar case was attributed to fat embolism,[2] but, occurring after what the manufacturers pointed out was a faster than recommended infusion,[3] may perhaps have represented a fat-overload syndrome. Neurological complications can be the presenting and principal signs of fat overload; focal and generalised seizures, weakness, and encephalopathy have been reported.[4]

Migraine with visual aura has also been reported in a 57-year old man taking soya beans, soya milk, and a soya protein supplement.[5]

1. Jellinek EH. Dangers of intravenous fat infusions. *Lancet* 1976; **ii:** 967.
2. Estebe JP, Malledant Y. Fat embolism after lipid emulsion infusion. *Lancet* 1991; **337:** 673.
3. McCracken M. Fat embolism after lipid emulsion infusion. *Lancet* 1991; **337:** 983.
4. Schulz PE, *et al.* Neurological complications from fat emulsion therapy. *Ann Neurol* 1994; **35:** 628–30.
5. Engel PA. New onset migraine associated with use of soy isoflavone supplements. *Neurology* 2002; **59:** 1289–90.

Hypersensitivity. Urticaria has been reported in 2 patients after the intravenous use of soya oil emulsions.[1,2] In one case the patient had previously received the emulsion for 19 days without ill-effect.[1]

Anaphylactic reactions have been documented after the ingestion of several foods or foodstuffs containing, or prepared from, soya beans, although the exact allergen remains unknown. In one patient who suffered anaphylactic attacks after eating such products a specific IgE-antibody response to the allergen Kunitz soybean trypsin inhibitor was demonstrated.[3] This was not, however, the only allergen present in soya beans as other patients who had a negative response to this allergen had positive responses in whole soya bean tests. A type I reaction to soya bean protein has been described in patients given parenteral lipid emulsions containing soya bean lecithin as the emulsifier.[4] A patient who ingested a soya protein drink experienced exercise-induced anaphylaxis; skin prick tests were positive to soya, but specific IgE antibodies to soya were undetectable.[5]

IgE antibodies to soya bean antigens have also been found in workers who suffered from asthma after handling soya beans[6,7] leading to the suggestion that an allergic mechanism had been responsible; the asthma was believed to have been due to the dust released during the handling of the beans.

1. Kamath KR, *et al.* Acute hypersensitivity reaction to Intralipid. *N Engl J Med* 1981; **304:** 360.
2. Hiyama DT, *et al.* Hypersensitivity following lipid emulsion infusion in an adult patient. *J Parenter Enteral Nutr* 1989; **13:** 318–20.
3. Moroz LA, Yang WH. Kunitz soybean trypsin inhibitor: a specific allergen in food anaphylaxis. *N Engl J Med* 1980; **302:** 1126–8.
4. Weidmann B, *et al.* Hypersensitivity reactions to parenteral lipid solutions. *Support Care Cancer* 1997; **5:** 504–5.
5. Taramarcaz P, *et al.* Soy anaphylaxis. *Allergy* 2001; **56:** 792.
6. Sunyer J, *et al.* Case-control study of serum immunoglobulin-E antibodies reactive with soybean in epidemic asthma. *Lancet* 1989; **i:** 179–82.
7. Hernando L, *et al.* Asthma epidemics and soybean in Cartagena (Spain). *Lancet* 1989; **i:** 502.

Pulmonary fat emboli. Pulmonary fat emboli or microemboli, sometimes fatal, have occurred in several infants who received infusions of fat emulsions based on soya oil.[1-3]

In one case[3] the patient's serum, which contained a high concentration of C-reactive protein, agglutinated the fat emulsion and this finding was considered to support the hypothesis that microemboli are formed by agglutination of fat emulsion in the blood by C-reactive protein. The authors of this report did not consider the precise pathogenesis to be clear, nor did they know whether the condition was preventable, but did suggest that it might be prudent either to ensure that the C-reactive protein concentration was normal (less than 10 mg/litre) or to perform a creaming test to determine which babies may embolise the infused fat emulsion. However, another study,[4] while not excluding a role of C-reactive protein in agglutination, failed to find any correlation between raised concentrations of this protein and the rate of agglutination. A review[5] classified fat embolism into those derived from direct entry of depot fat into the blood (e.g. after trauma), and those derived from agglutination of endogenous or exogenous fat. High concentrations of C-reactive protein were considered to be responsible for the agglutination of the liposomes of fat emulsions; chylomicrons and very low-density lipoproteins in the blood may also agglutinate, contributing to fat embolism.

1. Barson AJ, *et al.* Fat embolism in infancy after intravenous fat infusions. *Arch Dis Child* 1978; **53:** 218–23.
2. Levene MI, *et al.* Pulmonary fat accumulation after Intralipid infusion in the preterm infant. *Lancet* 1980; **ii:** 815–8.
3. Hulman G, Levene M. Intralipid microemboli. *Arch Dis Child* 1986; **61:** 702–3.
4. Zagara G, *et al.* C-reactive protein and serum agglutination in vivo of intravenous fat emulsions. *Lancet* 1989; **i:** 733.
5. Hulman G. The pathogenesis of fat embolism. *J Pathol* 1995; **176:** 3–9.

Precautions

Intravenous soya oil emulsion should not be given to patients with severe liver disease, acute shock, or severe or pathological hyperlipidaemia, or when the ability to metabolise fat may otherwise be impaired. Caution has also been advised in patients with pulmonary disease, renal insufficiency, uncompensated diabetes mellitus, metabolic disorders, sepsis, anaemia, and some disorders of blood coagulation. If given to such patients, the elimination of fat should be monitored daily.

Intravenous soya oil emulsion may interfere with some laboratory tests if blood is taken before fat has adequately cleared; this may take 4 to 6 hours.

Egg-yolk phospholipids may be used as emulsifiers in some preparations, which should not be given to patients with severe egg allergy.

Fat emulsions may extract phthalate plasticisers from bags and giving sets and non-phthalate containing equipment should be used wherever possible.

Soya-based infant feeds should be avoided in infants with documented cow's milk protein-induced enteropathy or enterocolitis, as these infants are often also sensitive to soya protein.

Neonatal hyperbilirubinaemia. In neonates with hyperbilirubinaemia, intravenous lipid emulsions should be used with caution because of the risk of displacing bilirubin from albumin. The risk appears to be higher in preterm infants,[1] at higher doses,[1] and with intermittent rather than continuous dosing.[2]

1. Spear ML, *et al.* The effect of 15-hour fat infusions of varying dosage on bilirubin binding to albumin. *J Parenter Enteral Nutr* 1985; **9:** 144–7.
2. Brans YW, *et al.* Influence of intravenous fat emulsion on serum bilirubin in very low birthweight neonates. *Arch Dis Child* 1987; **62:** 156–60.

Uses and Administration

Emulsions of fractionated soya oil containing 10, 20, or 30% are given by slow intravenous infusion as part of total parenteral nutrition regimens (p.1923), usually with amino acid and carbohydrate solutions. The solutions and emulsions may be given at separate sites, at the same site through a Y-connector, or combined in one admixture. Fat emulsions provide a high energy intake in a relatively small volume. They may also be used to prevent or correct essential fatty acid deficiency. When used as a calorie source the dose of the emulsion is determined by the energy requirements and clinical status of the patient; the amount of total carbohydrate, generally, should not comprise more than 60% of patients' total calorie intake. For the prevention and correction of fatty acid deficiency about 5 to 10% of total calorific intake should be as an intravenous fat emulsion.

The composition and dosage recommendations of commercial preparations do differ slightly but they should be started slowly. Suggested initial rates for the 10% and 20% products are 1 mL/minute and 0.5 mL/minute respectively for 15 to 30 minutes. The rate may then be increased and up to about 500 mL (or 10 mL/kg) of 10% or 250 mL (or 5 mL/kg) of 20% emulsion may be given on the first day. The total daily dosage may then be increased gradually on subsequent days; suggested daily dose ranges are 500 to 1500 mL of a 10% or 500 to 1000 mL of a 20% emulsion and

suggested rates of infusion are 500 mL of a 10% emulsion over a period of not less than 3 hours, and 500 mL of a 20% emulsion over not less than 5 hours. Where a 30% emulsion is used, a dose of 333 mL or about 4.75 mL/kg has been recommended, given over 5 hours or more; the first dose should not exceed 3 mL/kg.

Soya oil also has emollient properties and is used as a bath additive in the treatment of dry skin conditions.

Preparations made from whole soya beans, containing soya oil and soya protein, are used as the basis of lactose-free vegetable milks for infants and patients with lactose or similar disaccharide intolerance or with an allergy to cow's milk protein (see also below).

Administration. It has been suggested[1] that it is the concentration of phospholipid solubilisers, and particularly the excess present as free phospholipid liposomes, that determines the effect of lipid emulsions on plasma-lipid concentrations. In 20 premature infants requiring parenteral nutrition, infusion of up to 4 g/kg of fat daily as a 20% emulsion had less effect on plasma lipid concentrations than 2 g/kg daily as a 10% emulsion; the difference was thought to be due to the fact that the 20% emulsion was relatively liposome-poor, with a ratio of phospholipids to triglycerides of 0.06, whereas the liposome-rich 10% emulsion had a ratio of 0.12. The authors suggested that the 10% emulsion should not be used in preterm infants. Others noted similar results;[2] a 10% lipid emulsion with a reduced phospholipid content has, however, been reported to be relatively well tolerated in premature infants.[3]

For mention of the risk of kernicterus if lipid infusions are given to hyperbilirubinaemic neonates, see under Precautions, above.

1. Haumont D, *et al.* Effect of liposomal content of lipid emulsions on plasma lipid concentrations in low birth weight infants receiving parenteral nutrition. *J Pediatr* 1992; **121:** 759–63.
2. Cairns PA, *et al.* Tolerance of mixed lipid emulsion in neonates: effect of concentration. *Arch Dis Child Fetal Neonatal Ed* 1996; **75:** F113–F116.
3. Gohlke BC, *et al.* Serum lipids during parenteral nutrition with a 10% lipid emulsion with reduced phospholipid emulsifier content in premature infants. *J Pediatr Endocrinol Metab* 1997; **10:** 505–9.

Food intolerance. The American Academy of Pediatrics has recommended[1] that soya-based infant feeds are appropriate for use in galactosaemia and hereditary lactase deficiency, and documented allergy to cow's milk protein. However, infants with documented cow's milk protein enteropathy or enterocolitis should receive hydrolysed protein formula, as they are likely to be sensitive to soya protein. They concluded that soya-based infant feeds have no proven role in the prevention of atopic disease or in the management of infantile colic. In infants and children at high risk for developing food allergies or intolerance, a systematic review[2] found that there was no evidence that feeding with a soy formula compared to a cow's milk formula reduced the incidence of food allergies or intolerance.

The FDA has warned against the use of soya-based drinks intended for adults as the sole source for nutrition for infants.[3] It was stated that soya drinks can lead to severe protein and calorie malnutrition, multiple vitamin and mineral deficiency, and death in infants who receive no other source of nourishment, and should not be confused with soya-based infant formulas, which are specially formulated to meet the nutritional needs of infants.

For reference to the use of soya-based foods themselves causing allergic reactions, see under Hypersensitivity, above.

1. American Academy of Pediatrics. Soy protein-based formulas: recommendations for use in infant feeding. *Pediatrics* 1998; **101:** 148–53.
2. Osborn DA, Sinn J. Soy formula for prevention of allergy and food intolerance in infants. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 08/11/05).
3. Nightingale S. Warnings issued about practices, products: soy drink warning. *JAMA* 1985; **254:** 1428.

Hyperlipidaemias. Soya protein has been tried in the treatment of hyperlipidaemia (p.1169). Soya isoflavones such as genistein (p.2391) and daidzein (p.2391) can mimic oestrogen and should therefore have a beneficial effect on blood lipids.[1,2] Other constituents of soya protein, including fytic acid and saponins, may also contribute and thus intact soya protein may provide the maximum cholesterol-lowering effect.[2,3] A meta-analysis of controlled trials found that the substitution of soya protein for animal protein in the diet resulted in significant decreases in serum total cholesterol, low-density lipoprotein (LDL)-cholesterol, and triglyceride concentrations.[4] A subsequent systematic review of studies reached similar conclusions,[1] and the FDA considered that a low-fat diet including 25 g daily of soya protein might reduce the risk of ischaemic heart disease.[2] A later analysis by the American Heart Association[5] considered that cardiovascular benefit was very modest and appeared only when large amounts of animal protein were substituted with soya protein. The effect appeared to be more to do with a broader modification of diet than any effect of soya isoflavones. Soya protein does not appear to have a cholesterol-lowering effect in subjects with normal cholesterol concentrations,[2] although a small study found it to be beneficial in type 2 diabetes patients with near-normal lipid concentrations.[6]

1. Costa RL, Summa MA. Soy protein in the management of hyperlipidemia. *Ann Pharmacother* 2000; **34:** 931–5.
2. Erdman JW. Soy protein and cardiovascular disease: a statement for healthcare professionals from the Nutrition Committee of the AHA. *Circulation* 2000; **102:** 2555–9.
3. Demonty I, *et al.* Role of isoflavones in the hypocholesterolemic effect of soy. *Nutr Rev* 2003; **61:** 189–203.
4. Anderson JW, *et al.* Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995; **333:** 276–82.
5. Sacks FM, *et al.* Soy protein, isoflavones, and cardiovascular health: an American Heart Association Science Advisory for professionals from the Nutrition Committee. *Circulation* 2006; **113:** 1034–44.
6. Hermansen K, *et al.* Beneficial effects of a soy-based dietary supplement on lipid levels and cardiovascular risk markers in type 2 diabetic subjects. *Diabetes Care* 2001; **24:** 228–33.

Menopausal disorders. Soya contains phytoestrogens in the form of isoflavones, in particular genistein (p.2391) and daidzein (p.2391), which have been investigated for their oestrogen-modulating effects in the treatment of menopausal symptoms (p.2077).[1] It is thought that genistein may exert oestrogenic effects in the presence of low oestrogen concentrations, but that it may be anti-oestrogenic when concentrations of oestrogen are high.[2]

A small reduction in the incidence of hot flushes has been noted with soya isoflavone extract.[3] A systematic review,[4] however, concluded that phytoestrogens available as soya foods, soya extracts, or red clover extracts (p.2285) do not improve hot flushes or other menopausal symptoms.

Isoflavones may have a beneficial effect on cholesterol and lipid concentrations (see Hyperlipidaemias, above). Some epidemiological studies and *animal* data suggest that they may also provide protection against breast cancer.[1,2,5] However, phytoestrogens could also stimulate breast tumour growth due to oestrogenic activity.[6] These stimulating and inhibitory effects may be concentration-dependent; soya products contain only small amounts of phytoestrogens and it may be difficult to consume enough soy to have any beneficial effect on breast cancer growth.[7] A meta-analysis[8] concluded that soya intake may be associated with a small reduction in breast cancer risk, but that this result should be interpreted with caution due to confounding factors and a lack of dose response. Given the possibility of adverse effects, recommendations for high-dose soya isoflavone supplementation to prevent breast cancer or its recurrence are premature.

A few small studies have shown that soya isoflavones can decrease bone turnover, leading to speculation that they could be used to prevent osteoporosis (p.1084).[1] The effects of these isoflavones should be investigated in larger trials before they can be recommended as alternatives to conventional HRT.[5-7,9] (For the view that they may lack cardiovascular benefits see Hyperlipidaemias, above.) In a trial to investigate effects on cognitive function, bone mineral density, and plasma lipids in postmenopausal women, no differences were noted between soya protein containing isoflavones, and placebo.[10]

1. Vincent A, Fitzpatrick LA. Soy isoflavones: are they useful in menopause? *Mayo Clin Proc* 2000; **75:** 1174–84.
2. Goldwyn S, *et al.* Promotion of health by soy isoflavones: efficacy, benefit and safety concerns. *Drug Metabol Drug Interact* 2000; **17:** 261–89.
3. Upmalis DH, *et al.* Vasomotor symptom relief by soy isoflavone extract tablets in postmenopausal women: a multicenter, double-blind, randomized, placebo-controlled study. *Menopause* 2000; **7:** 236–42. Correction. *ibid.*; 422.
4. Krebs EE, *et al.* Phytoestrogens for treatment of menopausal symptoms: a systematic review. *Obstet Gynecol* 2004; **104:** 824–36.
5. Sirtori CR. Risks and benefits of soy phytoestrogens in cardiovascular diseases, cancer, climacteric symptoms and osteoporosis. *Drug Safety* 2001; **24:** 665–82.
6. Mason P. Isoflavones. *Pharm J* 2001; **266:** 16–19.
7. de Lemos ML. Effects of soy phytoestrogens genistein and daidzein on breast cancer growth. *Ann Pharmacother* 2001; **35:** 1118–21.
8. Trock BJ, *et al.* Meta-analysis of soy intake and breast cancer risk. *J Natl Cancer Inst* 2006; **98:** 459–71.
9. Anonymous. The role of isoflavones in menopausal health: consensus opinion of the North American Menopause Society. *Menopause* 2000; **7:** 215–29.
10. Kreijkamp-Kaspers S, *et al.* Effect of soy protein containing isoflavones on cognitive function, bone mineral density, and plasma lipids in postmenopausal women: a randomized controlled trial. *JAMA* 2004; **292:** 65–74.

Preparations

USP 31: Lipid Injectable Emulsion.

Proprietary Preparations (details are given in Part 3)

Arg.: Ivelip; Lipofundin N; Lipovenos; Piascledine; Sojar Pro; Soyacal; ***Austral.:*** Intralipid; Ivelip†; ***Austria:*** Balneum; Elolipid; Intralipid; Lipovenos; Olbad Cordes; ***Belg.:*** Gynosoya; ***Braz.:*** Endolipid†; Fisiogen; Isofarma†; ***Canad.:*** Intralipid; ***Chile:*** Lipofundin; Lipovenos; ***Cz.:*** Balneum Hermal; Elolipid†; Intralipid; Ivelip†; Lipofundin N†; Lipovenoes; Soyacal; ***Denm.:*** Intralipid; ***Fin.:*** Intralipid; ***Fr.:*** Endolipide†; Gastro'Aid; Gydrelle Phyto; Gynalpha; Intralipide; Ivelip; Phyto Soya; ***Ger.:*** Allergika†; Balneoconzen N; Balneovit; Balneum; Deltalipid; Eucerin Omega Olbad†; Intralipid; Lipofundin N; Lipopharm; Lipostabil; Lipovenos; Olbad Cordes; Penatoel†; salvilipid; Soyacal; ***Gr.:*** Intralipid; Lipovenoes†; ***Hong Kong:*** Intralipid; Lipofundin N; ***Hung.:*** Intralipid; Lipofundin; Lipovenos†; Structolipid; ***Indon.:*** Intralipos; ***Irl.:*** Balneum; Intralipid; ***Israel:*** Balneum; Intralipid; Ivelip; ***Ital.:*** Balneum Hermal; Elolipid; Intralipid; Ivelip†; Lipofundin S; Lipovenos; Soyacal†; ***Jpn:*** Intrafat†; ***Malaysia:*** Intralipid; Intralipos†; ***Mex.:*** Ivelip†; Lipofundin N; Lipovenoes; ***Neth.:*** Intralipid; Lipovenos; ***Norw.:*** Intralipid; ***NZ:*** Intralipid; Ivelip; ***Philipp.:*** Soyacal; ***Pol.:*** Balneum Hermal; Intralipid; Ivelip; Lipofundin N; Soya Meno; Soyfem; ***Port.:*** Banholeum; Emulsao de Lipidos; Endolipide; Intralipid; Lipovenoes; Soyacal; ***Singapore:*** Intralipid; Intralipos; ***Spain:*** Aquiflav; Bluna; Fitoladius; Flavodrei; Intralipid; Isodonna; Ivelip; Lipovenos; Malena; Phyto Soya; Pleginer; Primsoja; Soyacal; ***Swed.:*** Intralipid; Lipovenos†; ***Switz.:*** Balmed Hermal; Balmed Hermal Plus; Balneum Hermal†; Intralipid; Lipovenos; ***Thai.:*** Intralipid; Intralipos†; Ivelip; Lipofundin N; Lipofundin S; Lipovenoes†; ***Turk.:*** Intralipid; Ivelip; Lipovenos; ***UK:*** Balneum; Intralipid; Ivelip; Lipofundin; ***USA:*** Intralipid; Liposyn III; ***Venez.:*** Intralipid†; Ivelip; Lipofundin N†.

Multi-ingredient: ***Arg.:*** Clinoleic; Derrumal; Kabiven; Lipofundin MCT/LCT-E; Lipofundin MCT/LCT†; Liposomas; Sigmafem; Sojar Plus-Calcio; ***Austral.:*** Bioglan Mens Super Soy/Clover; Bioglan Soy Power Plus; Extralife Meno-Care; Hypol; Lifechange Menopause Formula†; PhytoLife; Soy Forte with Black Cohosh†; ***Austria:*** Balneum Plus; Clinoleic; Clinomel; Compleven†; Gesamtnahrlosung; KabiMix; Kabiven; Lipofundin mit MCT; Nutriflex Lipid; Olbad Cordes comp; Oleosint; OliClinomel; PE-Mix; SMOFlipid; Structolipid; TriMix; Vitromix; ***Belg.:*** Medialipide†; ***Braz.:*** Borag; Piascledine; ***Chile:*** Kabiven; Lipofundin MCT/LCT; Liposyn†; Lipovenos MCT/LCT; ***Cz.:*** Balneum Hermal Plus; Clinoleic; Clinomel†; Kabiven; Lipofundin MCT/LCT; Lipoplus; Nutralipid MCT†; Nutralipid P†; Nutriflex Lipid; OliClinomel; Piascledine; SMOFlipid; ***Denm.:*** Clinoleic; Kabiven; Liposyn†; OliClinomel; SMOFlipid; Vitrimix†; ***Fin.:*** Clinoleic; Compleven†; Kabiven; Lipoplus; Liposyn†; Nutriflex Lipid; OliClinomel; Structolipid; Vamin Glukos Combi†; Vasolipid; ***Fr.:*** Biopause; Biopause solution intime; Clinoleic; Clinomel†; Gynosoja; KabiMix†; Kabiven; Medialipide; Nutriflex Lipide; OliClinomel; Perikabiven; Piascledine; StructoKabiven; Structolipide; Vitrimix KV; ***Ger.:*** Abbolipid†; Balneum Plus; Clinoleic; Clinomel†; Compleven†; Kabiven; Lipofundin MCT; Lipovenos MCT; Nutriflex Lipid; Oleobal; OliClinomel; SMOFlipid; Sulfo-Olbad Cordes†; Windol Basisbad†; ***Gr.:*** Clinoleic; Clinomel; Kabiven; Lipofundin MCT/LCT; Nutriflex Lipid; OliClinomel; SMOFlipid; ***Hong Kong:*** Apaisac; Kabiven; Lipofundin MCT/LCT; Nutriflex Lipid; Sawmetto Vivo-Livo†; Vitrimix KV; ***Hung.:*** Clinomel†; Kabiven; Lipofundin MCT; Lipovenos PLR†; OliClinomel; SMOFlipid; ***Indon.:*** Hepabion; Ivelip; Kabiven; Lanaven; Lipofundin MCT/LCT; Lipovenoes; Maxitrin; Vitrimix; ***Irl.:*** Balneum Plus; Vitrimix KV; ***Israel:*** Balneum Plus; Clinoleic; Kabiven; Lipofundin MCT/LCT; Liposyn; ***Ital.:*** Acumel; Climil Complex; Climil-80; Clinoleic; Clinomel†; Demalit; Fitogen; Ginil; KabiMix†; Kabiven; Lipofundin MCT; Liposyn†; Nutriperi Lipid; Nutriplus Lipid; Nutrispecial Lipid; OliClinomel; Periven; Piascledine; Pluvio; Pulsalux; Sojyam†; Soymen; Structolipid; Triacid; Trivemil†; ***Malaysia:*** Kabiven; Vitrimix KV†; ***Mex.:*** Bano Coloide; Caltrate + S; Clinoleic†; Clinomel†; Kabiven; Lipofundin MCT/LCT; Liposyn; Lipovenoes MCT†; Piascledine; Riban; Soyaloid; Soyaloid Apruri; Soydex; Sy-Clinomel†; ***Neth.:*** Clinoleic; KabiMix†; Kabiven; Lipofundin MCT/LCT; Lipoplus; Nutriflex Lipid; OliClinomel; SMOFlipid; Structolipid; Vitrimix KV; ***Norw.:*** Ivamix†; KabiMix†; Kabiven; Nutriflex Lipid; SMOFlipid; Vasolipid; Vitrimix†; ***NZ:*** Kabiven; ***Philipp.:*** Her Soy Plus; ***Pol.:*** Balneum Hermal Plus; Clinoleic; Clinomel; Compleven; Kabiven; Lecigal†; Lipofundin MCT/LCT; Naturapia Menopauza; Piascledine; SMOFlipid; ***Port.:*** Banholeum Composto; Banholeum Gele; Clinoleic; Lipofundina MCT/LCT; Lipoplus; Nutribraun; Nutriplasmal; OliClinomel; Structolipid; Vitrimix; ***Rus.:*** Kabiven (Кабивен); Piascledine (Пиаскледин); ***S.Afr.:*** Clinomel; Lipofundin MCT/LCT; ***Singapore:*** Celatrac; Kabiven; Lipofundin MCT/LCT†; ***Spain:*** Clinoleic; Clinomel†; Fitogyn; KabiMix†; Kabiven; Lipofundina MCT/LCT; Nutriflex Lipid; Nutriplasmal†; OliClinomel; Structolipid; ***Swed.:*** Clinoleic; Clinomel†; Compleven†; KabiMix†; Kabiven; Lipoplus; Liposyn†; Nutriflex Lipid; OliClinomel; SMOFlipid; Structolipid; Vasolipid; Vitrimix†; ***Switz.:*** Antidry; Balneum Hermal Plus†; Clinoleic; Lipofundin MCT/LCT; Nutriflex Lipid; OliClinomel; Structolipid; ***Thai.:*** Kabiven; Lipofundin MCT/LCT; OliClinomel; Vitrimix; ***Turk.:*** Lipofundin MCT/LCT; Liposyn; Vitrimix; ***UK:*** Balneum Plus; Clinoleic; Compleven†; Kabiven; Lipidem; Lipofundin MCT/LCT; OliClinomel; Phytolife Plus; SMOFlipid; Structolipid; Vitrimix KV†; Ymea; ***USA:*** Liposyn II; Tucks; ***Venez.:*** Lipofundin MCT/LCT.

Stannous Fluoride

Fluoruro estañoso; Stannosi Fluoridum. Tin fluoride.

SnF_2 = 156.7.

CAS — 7783-47-3.

ATC — A01AA04.

ATC Vet — QA01AA04.

Pharmacopoeias. In *US*.

USP 31 (Stannous Fluoride). A white crystalline powder. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether. pH of a freshly prepared 0.4% solution in water is between 2.8 and 3.5.

Stability. Aqueous solutions of stannous fluoride decompose within a few hours with the formation of a white precipitate; they slowly attack glass.

Profile

Stannous fluoride is used as a source of fluoride (see Sodium Fluoride, p.1962) for the prophylaxis of dental caries. Dental gels containing concentrations of stannous fluoride 0.4% are available for daily use. Higher concentrations have been applied under professional supervision. Stannous fluoride has also been used in dentifrices and mouth rinses.

Stannous fluoride has an unpleasant taste.

Preparations

USP 31: Stannous Fluoride Gel.

Proprietary Preparations (details are given in Part 3)

Fr.: Emoform; ***Ital.:*** Fluorigard Gel-Kam; Gel-Kam†; Oral-B Pasta Dentificia Denti e Gengive; ***Switz.:*** Parocare†; ***UK:*** Fluorigard Gel-Kam; ***USA:*** Gel Kam; Gel-Kam; Gel-Tin; PerioMed; Stop.

Multi-ingredient: ***Fr.:*** Meridol†; ***Israel:*** Meridol; ***Ital.:*** Actifluor†.