der professional supervision. Formulations for children under 7 years of age typically contain sodium fluoride 0.11% (500 ppm); higher concentrations may be used, but the amount applied should be supervised to avoid excessive use or ingestion. Sodium fluoride has also been applied topically as a varnish under professional supervision. Alternatively, sodium fluoride solutions or gels acidified with phosphoric acid (commonly known as acidulated phosphate fluoride preparations) may be used. These preparations are considered to increase the fluoride uptake by the enamel and protect the enamel from demineralisation. For maximum benefit, eating, drinking, or rinsing should be avoided for at least 15 to 30 minutes after topical fluoride application.

Other fluoride compounds used in oral hygiene products and toothpastes include aluminium fluoride, ammonium fluoride, calcium fluoride (p.1932), dectaflur (p.1937), magnesium fluoride (p.1955) nicomethanol hydrofluoride, olaflur (p.1959), potassium fluoride, sodium monofluorophosphate (p.1964), and stannous fluoride (p.1967). Other fluorides used in the fluoridation of water supplies include sodium silicofluoride (p.1965).

Sodium fluoride has also been used, like some other fluoride compounds, in **rodenticides** and **insecticides**.

Dental caries prophylaxis. There is strong and consistent evidence in favour of the effectiveness of fluoride in preventing or reducing the incidence of dental caries. However, there is no strong evidence that one form of topical fluoride is more effective than another.

References.

1. WHO. Fluorides and oral health: report of a WHO expert committee on oral health status and fluoride use. *WHO Tech Rep Ser 846* 1994.
2. Anonymous. Fluoride supplement dosage: a statement by the British Dental Association, the British Society of Paediatric Dentistry and the British Association for the Study of Community Dentistry. *Br Dent J* 1997; **182:** 6–7.
3. Craig GC. Fluorides and the prevention of dental decay: a statement from the Representative Board of the British Dental Association. *Br Dent J* 2000; **188:** 654.
4. CDC. Recommendations for using fluoride to prevent and control dental caries in the United States. *MMWR* 2001; **50** (RR-14): 1–42. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5014.pdf (accessed 08/11/05)
5. Marinho VCC, *et al.* Fluoride gels for preventing dental caries in children and adolescents. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 08/11/05).
6. Marinho VCC, *et al.* Fluoride varnishes for preventing dental caries in children and adolescents. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 08/11/05).
7. Marinho VCC, *et al.* Fluoride toothpastes for preventing dental caries in children and adolescents. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2003 (accessed 08/11/05).
8. Marinho VCC, *et al.* Fluoride mouthrinses for preventing dental caries in children and adolescents. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2003 (accessed 08/11/05).
9. Twetman S, *et al.* Caries-preventive effect of fluoride toothpaste: a systematic review. *Acta Odontol Scand* 2003; **61:** 347–55.
10. Marinho VCC, *et al.* One topical fluoride (toothpastes, or mouthrinses, or gels, or varnishes) versus another for preventing dental caries in children and adolescents. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 08/11/05).
11. Marinho VCC, *et al.* Combinations of topical fluoride (toothpastes, mouthrinses, gels, varnishes) versus single topical fluoride for preventing dental caries in children and adolescents. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 08/11/05).
12. Petersson LG, *et al.* Professional fluoride varnish treatment for caries control: a systematic review of clinical trials. *Acta Odontol Scand* 2004; **62:** 170–6.
13. Twetman S, *et al.* Caries-preventive effect of sodium fluoride mouthrinses: a systematic review of controlled clinical trials. *Acta Odontol Scand* 2004; **62:** 223–30.
14. Jones S, *et al.* The effective use of fluorides in public health. *Bull WHO* 2005; **83:** 670–6.
15. WHO/FDI World Dental Federation/International Association for Dental Research. Global consultation on oral health through fluoride: call to action to promote dental health by using fluoride (issued November 2006). Available at: http://www.fdiworldental.org/public_health/assets/Fluoride_Consultation/Fluoride_Declaration_Final_E.pdf (accessed 10/03/08)
16. WHO/FDI World Dental Federation/International Association for Dental Research. Beijing declaration: call to action to promote oral health by using fluoride in China and Southeast Asia (issued September 2007). Available at: http://www.fdiworldental.org/public_health/assets/Fluoride_Consultation/Beijing_Declaration_English.pdf (accessed 10/03/08)

Fluoridation of water. Some countries add fluoride to water supplies to prevent dental caries. This has been the subject of much controversy.

References.

1. MRC. MRC working group report: water fluoridation and health (issued September 2002). Available at: http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002482 (accessed 10/03/08)
2. The British Fluoridation Society/The UK Public Health Association/The British Dental Association/The Faculty of Public Health. One in a million: the facts about water fluoridation. 2nd edition. Available at: http://www.bfsweb.org/onemillion/onemillion.htm (accessed 10/03/08)
3. Cheng KK, *et al.* Adding fluoride to water supplies. *BMJ* 2007; **335:** 699–702.

Human requirements. In the USA dietary reference intakes have been set for fluoride. These propose an adequate intake (see p.1925) for dental caries prevention to be 4 mg daily in adult men and 3 mg in women;[1] lower values are suggested in children and adolescents, depending on age. The tolerable upper intake level is 10 mg daily in adults.[1]

1. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride*. Washington, DC: National Academy Press, 1999. Also available at: http://www.nap.edu/openbook.php?isbn=0309063507 (accessed 21/07/08)

Osteoporosis. Fluoride has been used in the treatment of osteoporosis (p.1084) to improve bone strength by inducing subclinical fluorosis. The main effect of fluoride on the skeleton is to stimulate osteoblasts and increase trabecular bone mass. Because antiresorptive drugs cannot restore lost bone mass, this is potentially valuable in the treatment of osteoporosis. However, too much fluoride can increase bone fragility, and the overall effect of sodium fluoride on the incidence of fracture has not been established.

A controlled study in patients with postmenopausal osteoporosis[1] found that sodium fluoride 75 mg daily with a calcium supplement increased trabecular bone mass of the spine but did not reduce the incidence of vertebral fractures. Patients given sodium fluoride also had a higher incidence of nonvertebral fractures. An extension and re-analysis of the study,[2] however, showed that gradual increases in bone mass observed in patients taking lower doses of sodium fluoride (down to about 40 mg daily) were associated with a decrease in the incidence of fractures. A previous study[3] had reported a beneficial effect in vertebral fracture rate in patients with primary osteoporosis and at least one vertebral crush fracture. In this study sodium fluoride was given in a daily dose of 50 mg; calcium and vitamin D were also given. Interim analysis of a subsequent study using a slow-release formulation of sodium fluoride 50 mg daily taken intermittently with a regular calcium supplement showed a decrease in vertebral fractures of 50% at 2.5 years.[4] At 4 years the beneficial effect was sustained, the main effect being seen in a reduced incidence of new vertebral fractures;[5] no reduction was seen in the incidence of recurrent fractures but this study found no evidence of an increase in nonvertebral fractures. Some consider that low-dose fluoride can be of benefit in established postmenopausal osteoporosis, but the therapeutic window is narrow, and calcium and vitamin D must also be given to meet the calcium demand and avoid resorption of established bone.[6] A further double-blind study failed to show a reduction in vertebral fracture rates in women with osteoporosis treated with fluoride, and calcium and vitamin D compared with women who received only calcium and vitamin D.[7] This was despite a significant increase in bone mass density of the spine in the fluoride-treated groups. Fluoride regimens consisted of 50 mg enteric-coated sodium fluoride daily, or 150 or 200 mg sodium monofluorophosphate daily. In contrast, a further 4-year study found a decrease in vertebral fracture rates in women with moderate osteoporosis treated with sodium monofluorophosphate 156 mg daily plus calcium compared with those receiving calcium alone.[8]

A systematic review of 11 studies concluded that fluoride can increase bone mineral density at the lumbar spine, but this does not reduce the rate of vertebral fractures.[9] The authors of this review considered that fluoride should not be used in the first-line therapy of postmenopausal osteoporosis.

1. Riggs BL, *et al.* Effect of fluoride treatment on the fracture rate in postmenopausal women with osteoporosis. *N Engl J Med* 1990; **322:** 802–9.
2. Riggs BL, *et al.* Clinical trial of fluoride therapy in postmenopausal osteoporotic women: extended observations and additional analysis. *J Bone Miner Res* 1994; **9:** 265–75.
3. Mamelle N, *et al.* Risk-benefit ratio of sodium fluoride treatment in primary vertebral osteoporosis. *Lancet* 1988; **ii:** 361–5.
4. Pak CYC, *et al.* Slow-release sodium fluoride in the management of postmenopausal osteoporosis: a randomized controlled trial. *Ann Intern Med* 1994; **120:** 625–32.
5. Pak CYC, *et al.* Treatment of postmenopausal osteoporosis with slow-release sodium fluoride: final report of a randomized controlled trial. *Ann Intern Med* 1995; **123:** 401–8.
6. Anonymous. New drugs for osteoporosis. *Med Lett Drugs Ther* 1996; **38:** 1–3.
7. Meunier PJ, *et al.* Fluoride salts are no better at preventing new vertebral fractures than calcium-vitamin D in postmenopausal osteoporosis: the FAVOStudy. *Osteoporosis Int* 1998; **8:** 4–12.
8. Reginster JY, *et al.* The effect of sodium monofluorophosphate plus calcium on vertebral fracture rate in postmenopausal women with moderate osteoporosis: a randomized, controlled trial. *Ann Intern Med* 1998; **129:** 1–8.
9. Haguenauer D, *et al.* Fluoride for treating postmenopausal osteoporosis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2000 (accessed 08/11/05).

Preparations

BP 2008: Sodium Fluoride Mouthwash; Sodium Fluoride Oral Drops; Sodium Fluoride Oral Solution; Sodium Fluoride Tablets;
USP 31: Sodium Fluoride and Acidulated Phosphate Topical Solution; Sodium Fluoride and Phosphoric Acid Gel; Sodium Fluoride Oral Solution; Sodium Fluoride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Elgydium Junior; Elgydium Proteccion; Fluordent; Fluorogel; Fluorogel 2001; Fluoroplat; Naf Buches; Nafluor†; Pentafresh†; ***Austral.:*** Fluor†; Flurets; Neutrafluor; ***Austria:*** Duraphat; Fluodont; Zymafluor; ***Belg.:*** Fluodontyl†; Fluor; Procal†; Z-Fluor; ***Braz.:*** Fluornatrium†; Fluotrat; Primafluor†; ***Canad.:*** Fluor-A-Day; Fluoridrops†; Fluorinse; Fluoritabs†; Fluotic; Karidium†; Oral-B Anti-Cavity Dental Rinse; Oro-NaF; PDF; ***Chile:*** Caristop; Fluocaril Bi-Fluore; Gengisyl; Vitaflur; Vitis Pasta; ***Cz.:*** Fluocaril†; Fluossen†; Ossin†; Zymafluor; ***Denm.:*** Duraphat; Fluorette; ***Fin.:*** Duraphat; Fludent; Fluorilette; ***Fr.:*** Elgydium Junior; Elgydium Protection Caries; Elgyfluor Junior†; Elgyfluor†; Fluodontyl; Fluogum; Fluoplexe; Fluor Microsol†; Fluorex; Sanogyl†; Zymafluor; ***Ger.:*** Duraphat; Fluoretten; Fluoros; NaFril†; Ossin; Zymafluor; ***Gr.:*** Apoflux†; Duraphat; ***Hung.:*** Arthrofluor; Dentocar; Zymafluor; ***India:*** Otoflour; ***Indon.:*** Listermint; ***Israel:*** Denticare†; Dentix; Duraphat; Fluden; Fluvium; Teeth Tough; Zymafluor; ***Ital.:*** AZ Verde; Dentosan Extra Fluor; Dentosan Prevent†; Duraphat; Eburdent; Fluor Verde; Fluor-In; Listerine Difesa; Oral-B Collutorio Protezione Anti-Carie Fluorinse; Zymafluor; ***Mex.:*** Audifluor; ***Neth.:*** Dentigel; En-De-Kay; Osteofluor; Zymafluor; ***Norw.:*** Duraphat; Fluorette; Flux; ***Philipp.:*** Infaflor; ***Pol.:*** Fluossen; Zymafluor; ***Port.:*** Duraphat; Elmex; Fluor-In; Maxfluor; Medusit†; Oratol F†; Zymafluor; ***Rus.:*** Ossin (Оссин)†; ***S.Afr.:*** Listerfluor; Zymafluor; ***Spain:*** Fluodontyl; Fluor; Zymafluor†; ***Swed.:*** Dentan; Dentirol Fluor; Duraphat†; Fludent; Fluorette; Top dent fluor; ***Switz.:*** Duraphat; Fluocaril†; Ossin; Ossofluor; Zymafluor; ***Thai.:*** Zymafluor; ***Turk.:*** Fluoxytil; Zymafluor; ***UK:*** Duraphat; En-De-Kay; Fluor-A-Day; Fluorigard; Sensodyne Mint; ***USA:*** ACT; APF†; Denta Plus; DentaGel; EtheDent; Fluorigard; Fluorinse; Fluoritab; Flura; Karidium; Karigel; Karigel-N; Listerine Tooth Defense; Luride; Minute-Gel; MouthKote F/R; NeutraGard Advanced; OrthoWash; Pediaflor; Pharmaflur; Phos-Flur; Point-Two; Prevident; SF Gel; Thera-Flur.

Multi-ingredient: ***Arg.:*** ADC Fluor; Buclorhex; Cal-C-Vita Fluor; Desensyl; Elgydium; Elgydium Dientes Sensibles; Elgyfluor†; Emoform Total; Esmedent con Fluor; Fluordent PX; Fluorexidina†; Fluorogel 2001 Chiquitos; Fluorogel 2001 para Dientes Sensibles; Hyper Sensitive; Odol Control Sarro†; Odol Med Antiplaca†; Odol Tratamiento de Encias†; Oral-B Dientes Sensibles con Fluor†; Oral-B Enjuague Bucal†; Parodontax Fluor; Sens-Out†; Sensigel; Sensodyne Antisarro; Sensodyne Bicarbonato de Sodio; Sensodyne Proteccion Total; Squam; Tri-Vi-Fluor; ***Austral.:*** Macleans Sensitive; Oral-B Sensitive†; ***Austria:*** Elmex; Ossiplex; ***Belg.:*** Elmex; Fluocaril; Sedemol; Sulfa-Sedemol; ***Braz.:*** Calcifix B12; Calcifix Irradiado; Calcigenol; Calcinol Complexo; Malvatricin; Malvatricin Branqueador; Malvatricin Natural; Poly-Vi-Fluor; Proplax†; Sensodyne Antitartaro; Sensodyne C/Bicarbonato de Sodio; Sensodyne Cool; Sensodyne Fresh Mint; Sensodyne Protecao Total; Tri-Vi-Fluor; ***Canad.:*** Cepacol with Fluoride; Oral Plan†; Oral-B Anti-Bacterial with Fluoride; Oral-B Sensitive†; Sensodyne-F; Tri-Vi-Flor†; ***Chile:*** Cariax; Caristop; FKD; Kariax†; Listermint Con Fluor; Oralgene; Orthokin; Ortodent†; Sensaid; Vitis Encias Pasta; ***Cz.:*** Bifluorid†; Blend-a-Med†; Elmex; Fluocaril Bi-Fluore Vitamin E†; Fluocaril Bi-Fluore†; Natabec F†; Ossiplex†; ***Denm.:*** Bifluorid; ***Fin.:*** Elmex; Xerodent; ***Fr.:*** Elgydium Dents Sensibiles; Elgyfluor†; Elmex Sensitive†; Elmex†; Fluocaril Bi-Fluore; Fluocaril dents sensibles; Fluocaril Junior and Fluocaril Kids; Fluogel; Fluoselgine; Fluosterol; Listerine protection dents et gencives; Parogencyl prevention gencives; Paroplak; Sanogyl Fluo†; Sanogyl Junior†; Sanogyl†; Sensigel; Zymaduo; ***Ger.:*** D-Fluoretten; Elmex; Fluor-Vigantoletten; Lawefluor N†; Multifluorid; Natabec F†; Ossiplex; Ossofortin Plus; Zymafluor D; ***Hong Kong:*** Listerine Teeth and Gum Defence; ***Hung.:*** Elmex; Ossiplex†; ***Israel:*** Elmex; ***Ital.:*** Actifluor†; Actisens†; Aqua Emoform†; AZ Protezione Gengive; AZ Tartar Control; Benodent; Bifluorid†; Broxo al Fluoro; Broxodin†; Colgate Total; Dentosan Junior; Dentosan Placca & Carie; Dentosan Sensibile; Eburdent F; Elmex; Emoform Actisens†; Emoform-Tat†; Eudent con Glysan†; Fluocaril; Fluocaril Bi-Fluore; Lacalut; Oral-B Collutorio per la Protezione di Denti e Gengive; Oral-B Sensitive; Ossiplex†; Otofluor; Plax†; Ridiodent; ***Mex.:*** Fluoxytil; ***Neth.:*** Elmex; ***Norw.:*** Xerodent; ***Philipp.:*** Listerine Teeth & Gum Defense; Poly-Vi-Flor; Xylorinse; ***Pol.:*** Bifluorid; Fluormex; Fluoro-zel; ***Port.:*** Bexident; Biofluor Ortodoncia†; Biofluor Plus†; Biofluor Prevencao†; Biofluor Sensitive†; Fluocaril Bi-Fluore; ***Rus.:*** Elgyfluor (Эльгифлуор); Sensigel (Сенсигель); ***S.Afr.:*** Ossiplex; ***Singapore:*** 2Sensitive†; Elgyfluor; Sensigel; ***Spain:*** Vitagama Fluor; ***Swed.:*** Bifluorid; Xerodent; ***Switz.:*** Elmex; Fluocaril Bi-Fluore†; Paro aux fluorures d'amines Gelee; Parodontax F†; ***Thai.:*** Poly-Vi-Flor; ***Turk.:*** D-Flor; Kalsifluor; Nesgarin; Sensodyne-F Gel; ***UK:*** Dentyl pH; Hydrotab; Listermint with Fluoride; Macleans Mouthguard; Saliva Orthana; Sensodyne-F; ***USA:*** Adeflor M†; Apatate with Fluoride†; ControlRx; Florical; Fluoridex Daily Defense Sensitivity Relief; Mulvidren-F Softab; Poly-Vi-Flor; Polytabs-F; Sensitivity Protection Crest; Soluvite; Tri Vit with Fluoride†; Tri-Vi-Flor; Trivitamin Fluoride Drops; Vi-Daylin/F; ***Venez.:*** Sensodyne.

Sodium Monofluorophosphate

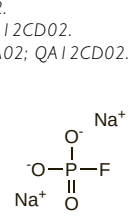
MFP Sodium; Monofluorofosfato sódico; Natrii Monofluorophosphas; Natriummonofluorfosfat; Natriummonofluorifosfaatti; Sodium Fluorophosphate. Disodium phosphorofluoridate.

Na_2PO_3F = 143.9.

CAS — 10163-15-2.

ATC — A01AA02; A12CD02.

ATC Vet — QA01AA02; QA12CD02.



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.

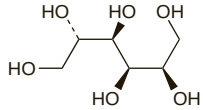
Profile
Sodium silicofluoride is used as a source of fluoride (see Sodium Fluoride, p.1962) for the fluoridation of drinking water. It has also been considered for inclusion in oral hygiene products.

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.