

Incompatibility. Polysorbates have been reported to be stable with electrolytes and weak acids and bases although saponification may occur in the presence of strong acids and bases. Discoloration or precipitation may occur with phenolic substances. The oleic acid esters are sensitive to oxidation. For reference to the possible incompatibility of polysorbate 80 with hydroxybenzoates, see p.1649.

Polysorbate 20 (BAN, USAN, INN)

E432; Monolaurato de polietileno 20 sorbitano; Monolaurato de polioxietileno 20 sorbitano; Polisorbat 20; Polisorbatas 20; Polisorbato 20; Polisorbát 20; Polyoxyethylene 20 Sorbitan Monolaurate; Polysorbaatti 20; Polysorbát 20; Polysorbat 20; Polysorbatum 20; Sorbimacrogol Laurate 300; Sorboxaethenum Laurinum.

Полисорбат 20

$C_{58}H_{114}O_{26}$ (approximate).
CAS — 9005-64-5.

Pharmacopoeias. In *Eur.* (see p.vii) and *Int.* Also in *USNF*.

Ph. Eur. 6.2 (Polysorbate 20). A mixture of partial esters of fatty acids, mainly lauric acid, with sorbitol and its anhydrides ethoxylated with about 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides. A clear or slightly opalescent yellowish to brownish-yellow oily liquid. Relative density about 1.10. Soluble in water, in dehydrated alcohol, in ethyl acetate, and in methyl alcohol; practically insoluble in liquid paraffin and in fatty oils. Store in airtight containers. Protect from light.

USNF 26 (Polysorbate 20). A laurate ester of sorbitol and its anhydrides copolymerised with approximately 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides. A lemon to amber liquid with a faint characteristic odour. Soluble in water, in alcohol, in dioxan, in ethyl acetate, and in methyl alcohol; insoluble in liquid paraffin. Store in airtight containers.

Polysorbate 40 (BAN, USAN, INN)

E434; Monopalmitato de polietileno 20 sorbitano; Monopalmitato de polioxietileno 20 sorbitano; Polisorbatas 40; Polisorbato 40; Polisorbát 40; Polyoxyethylene 20 Sorbitan Monopalmitate; Polysorbaatti 40; Polysorbát 40; Polysorbat 40; Polysorbatum 40; Sorbimacrogol Palmitate 300.

Полисорбат 40

$C_{62}H_{122}O_{26}$ (approximate).
CAS — 9005-66-7.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF*.

Ph. Eur. 6.2 (Polysorbate 40). Mixture of partial esters of fatty acids, mainly palmitic acid, with sorbitol and its anhydrides ethoxylated with about 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydrides. An oily, viscous, yellowish or brownish-yellow liquid. Relative density about 1.10. Miscible with water, with dehydrated alcohol, with ethyl acetate, and with methyl alcohol; practically insoluble in fatty oils and in liquid paraffin. Store in airtight containers. Protect from light. The BP 2008 gives Polyoxyethylene 20 Sorbitan Monopalmitate as an approved synonym.

USNF 26 (Polysorbate 40). A palmitate ester of sorbitol and its anhydrides copolymerised with about 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides. A yellow liquid with a faint characteristic odour. Soluble in water and in alcohol; insoluble in liquid paraffin and in vegetable oils. Store in airtight containers.

Polysorbate 60 (BAN, USAN, INN)

E435; Monoestearato de polietileno 20 sorbitano; Monoestearato de polioxietileno 20 sorbitano; Polisorbat 60; Polisorbatas 60; Polisorbato 60; Polisorbát 60; Polyoxyethylene 20 Sorbitan Monostearate; Polysorbaatti 60; Polysorbát 60; Polysorbat 60; Polysorbatum 60; Sorbimacrogol Stearate 300; Sorboxaethenum Stearinum.

Полисорбат 60

$C_{64}H_{126}O_{26}$ (approximate).
CAS — 9005-67-8.

Pharmacopoeias. In *Eur.* (see p.vii) and *Int.* Also in *USNF*.

Ph. Eur. 6.2 (Polysorbate 60). A mixture of partial esters of fatty acids, mainly stearic acid 50, with sorbitol and its anhydrides ethoxylated with about 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides. A yellowish-brown gelatinous mass which becomes a clear liquid at temperatures above 25°. Relative density about 1.10. Soluble in water, in dehydrated alcohol, in ethyl acetate, and in methyl alcohol; practically insoluble in liquid paraffin and in fatty oils. Store in airtight containers. Protect from light.

USNF 26 (Polysorbate 60). A mixture of stearate and palmitate esters of sorbitol and its anhydrides copolymerised with approximately 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides. A lemon to orange-coloured oily liquid or semi-gel with a faint characteristic odour. Soluble in water, in ethyl acetate, and in toluene; insoluble in liquid paraffin and in vegetable oils. Store in airtight containers.

The symbol † denotes a preparation no longer actively marketed

Polysorbate 80 (BAN, USAN, INN)

E433; Monooleato de polietileno 20 sorbitano; Monooleato de polioxietileno 20 sorbitano; Olethyan 20; Polisorbat 80; Polisorbatas 80; Polisorbato 80; Polisorbát 80; Polyäthylenglykol-Sorbitanoleat; Polyoxyethylene 20 Sorbitan Mono-oleate; Polysorbaatti 80; Polysorbát 80; Polysorbat 80; Polysorbatum 80; Polysorbitanum 80 Oleinatum; Sorbimacrogol Oleate 300; Sorboxaethenum Oleinicum; Sorethyan 20 Mono-oleate.

Полисорбат 80

$C_{64}H_{124}O_{26}$ (approximate).
CAS — 9005-65-6.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, and *Jpn.* Also in *USNF*.

Ph. Eur. 6.2 (Polysorbate 80). A mixture of partial esters of fatty acids, mainly oleic acid, with sorbitol and its anhydrides ethoxylated with about 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides. An oily, yellowish or brownish-yellow, clear or slightly opalescent liquid. Relative density about 1.10. Dispersible in water, in dehydrated alcohol, in ethyl acetate, and in methyl alcohol; practically insoluble in liquid paraffin and in fatty oils. Store in airtight containers. Protect from light.

USNF 26 (Polysorbate 80). An oleate ester of sorbitol and its anhydrides copolymerised with about 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides. A lemon to amber-coloured oily liquid with a faint characteristic odour. Sp. gr. between 1.06 and 1.09; viscosity, at 25°, between 300 and 500 mPa.s. Very soluble in water, producing an odourless and practically colourless solution; soluble in alcohol and in ethyl acetate; insoluble in liquid paraffin. Store in airtight containers.

Polysorbate 85 (BAN, USAN, INN)

Polisorbatas 85; Polisorbato 85; Polisorbát 85; Polyoxyethylene 20 Sorbitan Trioleate; Polysorbaatti 85; Polysorbat 85; Polysorbát 85; Polysorbatum 85; Sorbimacrogol Trioleate 300; Trioleato de polietileno 20 sorbitano; Trioleato de polioxietileno 20 sorbitano.

Полисорбат 85

$C_{100}H_{188}O_{28}$ (approximate).
CAS — 9005-70-3.

Description. A mixture of mainly trioleate esters of sorbitol and its anhydrides copolymerised with about 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides.

Adverse Effects and Precautions

Polysorbates may increase the absorption of fat-soluble substances.

There have been occasional reports of hypersensitivity after topical application of preparations containing polysorbates.

For discussion of fatalities in low-birth-weight infants associated with the injection of a polysorbate-containing preparation, see below.

Polysorbates used as excipients may also lead to adverse effects due to alterations in the pharmacokinetics of the formulated drug.

References

- ten Tije AJ, *et al.* Pharmacological effects of formulation vehicles: implications for cancer chemotherapy. *Clin Pharmacokinet* 2003; **42**: 665–85.

Effects in infants. After the introduction in the USA of an intravenous preparation of vitamin E (*E-Ferol*) there were a number of reports of unusual liver and kidney disorders, with 38 deaths being reported among treated low-birth-weight infants. Affected infants had unexplained hypotension, thrombocytopenia, renal dysfunction, hepatomegaly, cholestasis, ascites, and metabolic acidosis.^{1–3} The preparation was subsequently withdrawn from the market in April 1984 about 5 months after it was introduced. *In-vitro* evidence was produced showing that *E-Ferol* suppressed the response of human lymphocytes to phytohaemagglutinin. However, it was the mixture of polysorbates, polysorbate 20 and in particular polysorbate 80, that was shown to be responsible for this suppression rather than the α -tocopherol acetate component. Despite this *in-vitro* data, overwhelming infection was not a feature in the affected infants.² Large doses of polysorbates were unavoidably injected when *E-Ferol* was used and it was suggested that polysorbates may accumulate as a result of an alteration in the metabolism by low-birth-weight infants; polysorbate-induced alteration of membrane fluidity in cells of vessel walls may have led to changes in structure and function.²

- Alade SL, *et al.* Polysorbate 80 and E-Ferol toxicity. *Pediatrics* 1986; **77**: 593–7.
- Balistreri WF, *et al.* Lessons from the E-Ferol tragedy. *Pediatrics* 1986; **78**: 503–6.
- Golightly LK, *et al.* Pharmaceutical excipients: adverse effects associated with inactive ingredients in drug products. *Med Toxicol* 1988; **3**: 128–65 and 209–240.

Hypersensitivity. Local inflammatory reactions after intramuscular injection of a vitamin A preparation were considered¹ to be due to a hypersensitivity reaction to polysorbate 80, included as an excipient. Anaphylactoid reactions which occurred in 2 patients after treatment with omalizumab for 27 and 13 months respectively, were likely to be due to the polysorbate excipient and not to the monoclonal antibody itself.² The presence of polysorbate 80 in the injection may also contribute to hypersen-

sitivity reactions to docetaxel (see Adverse Effects of Docetaxel, p.710).

- Shelley WB, *et al.* Polysorbate 80 hypersensitivity. *Lancet* 1995; **345**: 1312–13.
- Price KS, Hamilton RG. Anaphylactoid reactions in two patients after omalizumab administration after successful long-term therapy. *Allergy Asthma Proc* 2007; **28**: 313–19.

Uses

Polysorbates are hydrophilic nonionic surfactants that are used as emulsifying agents for the preparation of stable oil-in-water emulsions in pharmaceutical products; they are frequently used with a sorbitan ester in varying proportions to produce products with a range of texture and consistency. Polysorbates have also been used in the formulation of insecticide and herbicide sprays, industrial detergents, and cosmetic products. They are also used as emulsifiers in the food industry.

Polysorbates are used as solubilising agents for a variety of substances including essential oils and oil-soluble vitamins such as vitamins A, D, and E, and as wetting agents in the formulation of oral and parenteral suspensions. However, hypersensitivity reactions have been attributed to the presence of polysorbates, see Hypersensitivity, above.

Polysorbates may also be used for their surfactant properties in preparations for the removal of ear wax, and for the management of dry eyes and upper respiratory-tract disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Sinroncar; **Belg.:** Oleosorbate; **Canad.:** Dioptears; Tears Encore; **Fr.:** Cerumenol; **USA:** OptiZen; Viva-Drops.

Multi-ingredient: **Arg.:** Balsan†; Otodean; Gotas Oticas; **Fin.:** Expigen; **Fr.:** Ceruspray; Fluisedal; Fluisedal sans promethazine; Paroplak; Prorhinel; **S.Afr.:** Expigen; **Switz.:** Prorhinel; Rhinocure; Rhinocure simplex; **Turk.:** Kanslak; Libalaks; **UK:** Asonor; **USA:** Refresh Dry Eye Therapy; Soothe; Soothe XP.

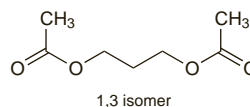
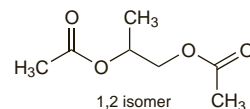
Propylene Glycol Diacetate

Propilenglicol, diacetato de. Propenediol diacetate.

Дицетат Пропиленгликоля

$C_7H_{12}O_4$ = 160.2.

CAS — 623-84-7 (1,2-isomer); 628-66-0 (1,3-isomer).



Profile

Propylene glycol diacetate is an emulsifying and/or solubilising agent, and a solvent. It is included in some external preparations for ear infection.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Canad.:** VoSol HC†; **NZ:** VoSol; **USA:** Acetasol; Acetasol HC; VoSol HC†; VoSol†.

Propylene Glycol Laurates

E477 (propylene glycol esters of fatty acids); Propilenglicol, laurato de.

Пропиленгликоля Лаураты

Propylene Glycol Dilaurate

E477 (propylene glycol esters of fatty acids); Propilenglicol, dilaurato de; Propilenglikolio dilauratas; Propyleeniglykolidilauraatti; Propylene Dilaurate; Propylenglycol, dilaurate de; Propylenglycoli dilauras; Propylenglykoldilaurat; Propylenglykol-dilaurát.

Пропиленгликоля Дилаурат

CAS — 22788-19-8.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF*.

Ph. Eur. 6.2 (Propylene Glycol Dilaurate). A mixture of the propylene glycol mono- and di-esters of lauric acid. It contains a minimum of 70% of di-esters and a maximum of 30% of mono-esters. The content of free propylene glycol is not more than 2%. A colourless or slightly yellow, clear oily liquid at 20°. Practically insoluble in water; very soluble in alcohol, in methyl alcohol, and in dichloromethane. Protect from moisture.

USNF 26 (Propylene Glycol Dilaurate). A mixture of the propylene glycol mono- and di-esters of lauric acid. It contains not less than 70.0% of di-esters and not more than 30.0% of mono-esters. Protect from moisture.