



Martindale

Thirty-sixth edition

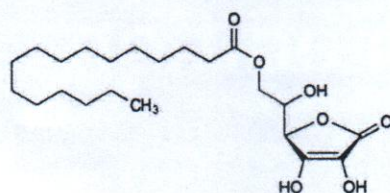
THE
COMPLETE
DRUG
REFERENCE

Fr.: Strepsils; Strepsils Lidocaine; Strepsils Miel-Citron; Strepsils Vitamine C; Strepsils Spray Lidocaine; Ger.: Dobendan Synergie; Neo-Angin; Gr.: Strepsils; Hong Kong: Strepsils Dual Action; Hung.: Neo-Angin; Strepsils; Strepsils Menthol and Eucalyptus; Strepsils Plus; Strepsils Vitamin C; Indon.: Col Q; Colisil; Ir.: Strepsils; Strepsils + Plus Anaesthetic; Strepsils Dual Action; Strepsils Vitamin C; Israel: Strepsils; Strepsils Plus; Strepsils with Menthol and Eucalyptus; Strepsils with Vitamin C; Ital.: Benagol; Benagol Mentolo-Eucalyptolo; Benagol Vitamina C; Malaysia: Chericof; Strepsils; Strepsils Dual Action; Net.: Strepsils; Strepsils Menthol en Eucalyptus; Strepsils Sinaasappel en Vitamine C; NZ: Strepsils; Strepsils Plus Anaesthetic; Strepsils with Vitamin C; Philipp.: Strepsils; Pol.: Neo-Angin; Strepsils; Rus.: Astrasept (Acrapcent); Coldact Loripils (Колдакт Лорпилс); Rinza Lorsept (Ринза Лорсепт); Strepsils (Стрепсилс); Strepsils Plus (Стрепсилс Плюс); Suprima-Lor (Суприма-Лор); S.Afr.: Strepsils; Strepsils Eucalyptus Menthol; Strepsils Orange-C; Strepsils Plus; Strepsils Soothing Honey & Lemon; Singapore: Strepsils; Strepsils Dual Action; Spain: Strepsils; Strepsils con Vitamina C; Strepsils Lidocaine; Swed.: Strepsils; Switz.: Neo-Angin au miel et citron; Neo-Angin avec vitamin C sans sucre; Neo-Angin sans sucre; Thai: Strepsils Butter Menthol Capsicum; Strepsils Plus Anaesthetic; Strepsils Plus Vit C; Strepsils Sugar Free; Throatit; Turk.: Strepsils C; Strepsils Mentollu; UK: Strepsils; Strepsils with Vitamin C.

Ascorbyl Palmitate

Ascorbilo, palmitato de; Ascorbyle, palmitate d'; Ascorbyls palmitat; Ascorbilo palmitatas; Ascorbylpalmitat; Ascorbylpalmitat; Ascorbylu palmitinyan; Ascorbylpalmitaatti; Ascorbilo palmitat; Vitamin C Palmitate; L-Ascorbic acid 6-hexadecanoate; L-Ascorbic acid 6-palmitate; 3-Oxo-L-gulofuranolactone 6-palmitate.

C₂₂H₃₈O₇ = 414.5.
CAS — 137-66-6.



NOTE. The code E304 is used for fatty acid esters of ascorbic acid, which include ascorbyl palmitate.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF*. **Ph. Eur.** 6.2 (Ascorbyl Palmitate). A white or yellowish-white powder. Practically insoluble in water, freely soluble in alcohol and in methyl alcohol, practically insoluble in dichloromethane and in fatty oils. Store in airtight containers. Protect from light. **USNF 26** (Ascorbyl Palmitate). A white to yellowish-white powder with a characteristic odour. Very slightly soluble in water, in chloroform, in ether, and in vegetable oils; soluble 1 in 125 of alcohol. Store at 8° to 15° in airtight containers.

Profile

Ascorbyl palmitate is an antioxidant used as a preservative in pharmaceutical products and foods. It is often used with alpha tocopherol (p.1992), and this combination shows marked synergy. As it is a fat-soluble derivative of vitamin C (ascorbic acid, p.1983), ascorbyl palmitate is sometimes used as a source of vitamin C in nutritional supplements.

Preparations

Proprietary Preparations (details are given in Part 3)
Chile: Neolud-C.

Multi-ingredients Hong Kong: Proflavanol; **Malaysia:** Proflavanol; **Port:** Thiospot; **Singapore:** Proflavanol.

Benzalkonium Chloride (BAN, INN)

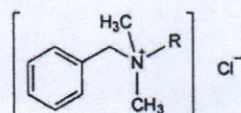
Benzalkoniumchlorid; Bentsalkoniumchlorid; Benzalkonio Chloruro; Benzalkonii chloridum; Benzalkonio chloridas; Benzalkoniowy chlorek; Benzalkonium Chloratum; Benzalkonium, chlorure de; Benzalkonium-chlorid; Benzalkonium-klorid; Benzalkonium Klor-ür; Cloreto de Benzalkonio; Cloruro de benzalkonio.

Бензалькони Хлорид

CAS — 8001-54-5.

ATC — D08AJ01; D09AA11; R02AA16.

ATC Vet — QD08AJ01; QD09AA11; QR02AA16.



R = C₈H₁₇ to C₁₈H₃₇

The symbol † denotes a preparation no longer actively marketed

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, and *Jpn.* Also in *USNF*. Some pharmacopoeias also have a monograph for a solution.

Chin. also includes benzalkonium bromide.

Ph. Eur. 6.2 (Benzalkonium Chloride). A mixture of alkylbenzyltrimethylammonium chlorides, the alkyl groups having chain lengths of C₈ to C₁₈. It contains not less than 95% and not more than 104% of alkylbenzyltrimethylammonium chlorides, calculated as C₂₂H₄₀ClN with reference to the anhydrous substance. A white or yellowish-white powder, or gelatinous yellowish-white pieces, hygroscopic and soapy to the touch. It forms a clear molten mass on heating. It contains not more than 10% of water. Very soluble in water and in alcohol. An aqueous solution froths copiously when shaken.

USNF 26 (Benzalkonium Chloride). A mixture of alkylbenzyltrimethylammonium chlorides of the general formula [C₆H₅CH₂N(CH₃)₃R]Cl, in which R represents a mixture of the alkyls having chain lengths from C₈ to C₁₆. It contains not less than 40% of the C₁₂H₂₅ compound, calculated on the anhydrous substance, not less than 20% of the C₁₄H₂₉ compound, and not less than 70% of the 2 compounds together.

A white or yellowish-white, thick gel, or gelatinous pieces with a mild aromatic odour. It contains not more than 15% of water. Very soluble in water and in alcohol; the anhydrous form is soluble 1 in 100 of ether and 1 in 6 of benzene. A solution in water is usually slightly alkaline and foams strongly when shaken. Store in airtight containers.

Incompatibility. Benzalkonium chloride is incompatible with soaps and other anionic surfactants, citrates, iodides, nitrates, permanganates, salicylates, silver salts, tartrates, and zinc oxide and sulfate. Incompatibilities have been demonstrated with ingredients of some commercial rubber mixes or plastics. Incompatibilities have also been reported with other substances including aluminium, cotton dressings, fluorescein sodium, hydrogen peroxide, hypromellose, kaolin, hydrous wool fat, and some sulfonamides.

Adverse Effects, Treatment, and Precautions

As for Cetrimide, p.1634. Because some rubbers are incompatible with benzalkonium chloride silicone rubber teats should be used on eye drop containers unless the suitability has been established.

Catheters and cannulas. For reference to benzalkonium chloride used in the manufacturing process of heparin-bonded catheters interfering with determination of serum concentrations of sodium and potassium, see under Precautions for Heparin, p.1303.

Effects on the eyes. Benzalkonium chloride is one of the most disruptive ophthalmic additives to the stability of the lipid film and to corneal epithelial membranes; toxicity studies have tended to be carried out using relatively high concentrations of benzalkonium chloride¹ but damage to the tear film and corneal conjunctival surface have been noted in patients receiving regular long-term treatment for glaucoma with eye drops preserved with benzalkonium chloride in usual concentrations.^{3,4}

Corneal toxicity has also been reported in patients inadvertently exposed to benzalkonium chloride as a preservative in viscoelastic material during cataract surgery.⁵ The use of preservatives in eye drops should generally be avoided and the formulation of such preparations in single-dose containers is desirable.^{1,2} Benzalkonium chloride is not suitable for use in solutions for storing and washing hydrophilic soft contact lenses, as it can bind to the lenses and may later produce ocular toxicity when the lenses are worn.⁶ Similarly, benzalkonium chloride use in anaesthetic eye drops is discouraged, as the anaesthetic component reduces the blink reflex and increases the contact time with the eye drops which may consequently result in increased toxicity due to the preservative. Patients with dry eye syndrome are also at increased risk of toxicity as the corneal epithelium is exposed to the full strength of the eye drops, in addition to which these patients do not produce enough tears to dilute the preservative in the eye drops.

- Burstein NL. The effects of topical drugs and preservatives on the tears and corneal epithelium in dry eye. *Trans Ophthalmol Soc UK* 1985; 104: 402-9.
- Burstein NL. Corneal cytotoxicity of topically applied drugs, vehicles and preservatives. *Surv Ophthalmol* 1980; 25: 15-30.
- Herreras JM, et al. Ocular surface alteration after long-term treatment with an antiglaucomatous drug. *Ophthalmology* 1992; 99: 1082-8.
- Kuppens EVMJ, et al. Effect of timolol with and without preservative on the basal tear turnover in glaucoma. *Br J Ophthalmol* 1995; 79: 339-42.
- Eleftheriadis H, et al. Corneal toxicity secondary to inadvertent use of benzalkonium chloride preserved viscoelastic material in cataract surgery. *Br J Ophthalmol* 2002; 86: 299-305.
- Gasset AR. Benzalkonium chloride toxicity to the human cornea. *Am J Ophthalmol* 1977; 84: 169-71.

Effects on the respiratory tract. Hypersensitivity to benzalkonium chloride, used as a preservative in nasal drops, was confirmed in a patient by a challenge that produced nasal congestion

and irritation of the eyes and throat lasting 48 hours.¹ A review² of 18 studies (14 *in vivo*, 4 *in vitro*) where benzalkonium chloride was used as the preservative in multidose nasal products found that 8 studies (all *in vivo*) found no toxic effects, while 10 reported degenerative changes to the nasal epithelia or exacerbation of rhinitis medicamentosa. However, in only 2 of these 10 studies were the differences between benzalkonium chloride and control groups found to be significant, and both of these included the use of oxymetazoline, which is known to cause rhinitis medicamentosa.

Benzalkonium chloride used as a preservative in nebulised solutions of anti-asthma drugs has been reported to cause dose-related bronchoconstriction especially in asthmatic patients,³ and has been associated with the precipitation of respiratory arrest.⁴

- Hillerdal G. Adverse reaction to locally applied preservatives in nose drops. *ORL J Otorhinolaryngol Relat Spec* 1985; 47: 278-9.
- Marple B, et al. Safety review of benzalkonium chloride used as a preservative in intranasal solutions: an overview of conflicting data and opinions. *Otolaryngol Head Neck Surg* 2004; 130: 131-41.
- Committee on Drugs, American Academy of Pediatrics. "Inactive" ingredients in pharmaceutical products: update. *Pediatrics* 1997; 99: 268-78.
- Boucher M, et al. Possible association of benzalkonium chloride in nebulizer solutions with respiratory arrest. *Ann Pharmacother* 1992; 26: 772-4.

Interactions

Benzalkonium chloride is not suitable for use in eye drops containing local anaesthetics (see Effects on the Eyes, above).

Uses and Administration

Benzalkonium chloride is a quaternary ammonium antiseptic and disinfectant with actions and uses similar to those of the other cationic surfactants (see Cetrimide, p.1634). It is also used as an antimicrobial preservative for pharmaceutical products. Benzalkonium bromide and benzalkonium saccharinate have also been used.

Solutions of benzalkonium chloride 0.01 to 0.1% are used for cleansing skin, mucous membranes, and wounds. More dilute solutions of 0.005% are suitable for irrigation of deep wounds. A 0.02 to 0.05% solution has been used as a vaginal douche. An aqueous solution containing 0.005 to 0.02% has been used for irrigation of the bladder and urethra and a 0.0025 to 0.005% solution for retention lavage of the bladder.

Creams containing benzalkonium chloride are used in the treatment of napkin rash and other dermatoses.

A 0.2 to 0.5% solution has been used as a shampoo in seborrhoeic dermatitis.

Lozenges containing benzalkonium chloride are used for the treatment of superficial infections of the mouth and throat.

Benzalkonium chloride is used as a preservative in ophthalmic solutions at a concentration of 0.01 to 0.02%, and in nasal and otic solutions at a concentration of 0.002 to 0.02%. Benzalkonium chloride is used for disinfecting rigid contact lenses (p.1622) but is unsuitable as a preservative in solutions for washing and storing hydrophilic soft contact lenses (see also Effects on the Eyes, above).

Benzalkonium chloride is also used as a spermicide.

Solutions of 0.13% are used for disinfection and storage of surgical instruments, sometimes with the addition of sodium nitrite to inhibit rust.

Action. The antibacterial effect of benzalkonium chloride 0.003% was enhanced by 0.175% of benzyl alcohol, phenylpropanol, or phenethyl alcohol.¹ For the use of phenethyl alcohol with benzalkonium chloride as a preservative for ophthalmic solutions, see Antimicrobial Action, under Phenethyl Alcohol, p.1655.

1. Richards RME, McBride RJ. Enhancement of benzalkonium chloride and chlorhexidine acetate activity against *Pseudomonas aeruginosa* by aromatic alcohols. *J Pharm Sci* 1973; 62: 2035-7.

Catheter-related sepsis. Benzalkonium chloride has been investigated^{1,2} for incorporation into catheters to reduce catheter-related sepsis (p.1624).

- Tebbs SE, Elliott TSJ. A novel, antimicrobial central venous catheter impregnated with benzalkonium chloride. *J Antimicrob Chemother* 1993; 31: 261-71.
- Moss HA, et al. A central venous catheter coated with benzalkonium chloride for the prevention of catheter-related microbial colonization. *Eur J Anaesthesiol* 2000; 17: 680-7.

1. Green TP, et al. Disposition of sodium benzoate in newborn infants with hyperammonemia. *J Pediatr* 1983; 102: 785-90.