water and in alcohol; slightly soluble in glycerol and in liquid paraffin. A 1% solution in water has a pH of 5.0 to 7.0. Protect from light.

Incompatibility. The activity of bronopol can be reduced by sodium metabisulfite, sodium thiosulfate, cysteine hydrochloride, and compounds with a thiol group. Incompatibility with unprotected aluminium affects packaging.

Stability. The stability of bronopol is affected by increases in temperature and by increases in pH above 8.

Creams and shampoos containing bronopol 0.01% as a preservative were found to contain free nitrite and, as a result of amines present in the preparations, nitrosamines.[1] It was recommended that nitrosamine formation could be reduced in preparations containing amines and bronopol by limiting the bronopol concentration to 0.01% and inclusion of alpha tocopherol 0.2% or butylated hydroxytoluene 0.05%.

1. Dunnett PC, Telling GM. Study of the fate of bronopol and the effects of antioxidants on N-nitrosamine formation in shampoos and skin creams. *Int J Cosmet Sci* 1984; **6:** 241–7.

Adverse Effects
Bronopol may be irritant when applied topically and cases of contact dermatitis have been reported.

Pharmacokinetics
Bronopol is absorbed following topical use.

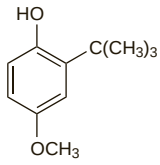
Uses
Bronopol is active against a wide range of bacteria, including *Pseudomonas aeruginosa*, but is less active against moulds and yeasts. Bronopol is used as a preservative in shampoos, cosmetics, and both topical and oral pharmaceutical preparations; concentrations in pharmaceutical preparations range from 0.01 to 0.1%, with the usual concentration being 0.02%. It is also used for its antimicrobial properties in various industrial applications, including in air conditioning systems.

Butylated Hydroxyanisole *(BAN)*

BHA; Butilhidroksianizolas; Butilhidroxianisol; Butil-hidroxianizol; Butilidrossianisolo; Butylhydroxianisol; Butylhydroxyanisol; Butylhydroxyanisole; Butylhydroxyanisolum; Butylohydroksyanizol; Butyylihydroksianisoli; E320. 2-*tert*-Butyl-4-methoxyphenol; 2-(1,1-dimethylethyl)-4-methoxyphenol.

$C_{11}H_{16}O_2$ = 180.2.

CAS — 25013-16-5.



Pharmacopoeias. In *Eur.* (see p.vii) and *Int.* Also in *USNF.*
Ph. Eur. 6.2 (Butylhydroxyanisole; Butylated Hydroxyanisole BP 2008). A white, yellowish, or slightly pinkish, crystalline powder. It contains not more than 10% of 3-(1,1-dimethylethyl)-4-methoxyphenol. Practically insoluble in water; freely soluble in alcohol and in fatty oils; very soluble in dichloromethane; it dissolves in dilute solutions of alkali hydroxides. Protect from light.
USNF 26 (Butylated Hydroxyanisole). A white, or slightly yellow, waxy solid with a faint characteristic odour. Insoluble in water; soluble 1 in 4 of alcohol, 1 in 2 of chloroform, and 1 in 1.2 of ether; freely soluble in propylene glycol.

Incompatibility. Butylated hydroxyanisole is incompatible with oxidising agents and ferric salts. Traces of metals can cause loss of activity.

Adverse Effects
Butylated hydroxyanisole can be irritant to the eyes, skin, and mucous membranes and can cause depigmentation. There are also reports of contact urticaria.

Carcinogenicity. There has been concern as to whether butylated hydroxyanisole may be a carcinogen.[1,2] These concerns stem from a study in which *rodents* given food containing 1 to 2% butylated hydroxyanisole developed squamous cell carcinoma of the forestomach. No similar malignancies were found in studies with *animals* that do not have a forestomach. The International Agency for Research on Cancer has concluded[2] that there is sufficient evidence for the carcinogenicity of butylated hydroxyanisole in *animals* but that there is no data on its carcinogenicity in humans.

1. FAO/WHO. Evaluation of certain food additives and contaminants: thirty-third report of the joint FAO/WHO expert committee on food additives. *WHO Tech Rep Ser 776* 1989. Available at: http://libdoc.who.int/trs/WHO_TRS_776.pdf (accessed 27/08/08)
2. IARC/WHO. Some naturally occurring and synthetic food components, furocoumarins and ultraviolet radiation. *IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans volume 40* 1986. Available at: http://monographs.iarc.fr/ENG/Monographs/vol40/volume40.pdf (accessed 23/05/06)

Effects on the blood. For a report of methaemoglobinaemia associated with the antoxidants (butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate) used to preserve the oil in a soybean infant feed, see under Adverse Effects in Alkyl Gallates (p.1628).

Pharmacokinetics
Butylated hydroxyanisole is absorbed from the gastrointestinal tract, then metabolised and conjugated, and excreted in the urine; less than 1% is excreted in the urine as unchanged drug within 24 hours of ingestion.

Uses
Butylated hydroxyanisole is an antoxidant with some antimicrobial activity. It is used as a preservative in cosmetics and foods as well as pharmaceutical preparations, particularly to delay or prevent oxidative rancidity of fats and oils in concentrations of up to 0.02%; higher concentrations have been used for essential oils. It is also used to prevent the loss of activity of oil-soluble vitamins. To improve efficacy, butylated hydroxyanisole is frequently used with other antoxidants such as butylated hydroxytoluene or an alkyl gallate and with sequestrants or synergists such as citric acid.

Commercial supplies of butylated hydroxyanisole used in food technology consist of mixtures of the 2-*tert* and 3-*tert* isomers.

Use in food. In the UK the Food Advisory Committee has recommended that the use of butylated hydroxyanisole and butylated hydroxytoluene should no longer be permitted as additives for infant formulas as they are no longer required for the economic manufacture of vitamin A and vitamin A esters.[1]

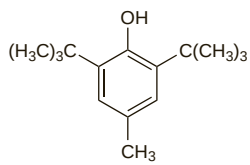
1. MAFF. Food Advisory Committee: report on the review of the use of additives in foods specially prepared for infants and young children. *FdAC/REP/12.* London: HMSO, 1992.

Butylated Hydroxytoluene *(BAN)*

BHT; Butilhidroksitoluenas; Butilhidroxitolueno; Butil-hidroxitoluol; Butylhydroxitoluen; Butylhydroxitoluenum; Butylhydroxytoluen; Butylhydroxytoluène; Butylhydroxytoluene; Butylhydroxytoluenum; Butylohydroksytoluen; Butyylihydroksitolueeni; E321. 2,6-Di-*tert*-butyl-*p*-cresol.

$C_{15}H_{24}O$ = 220.4.

CAS — 128-37-0.



Pharmacopoeias. In *Eur.* (see p.vii) and *Int.* Also in *USNF.*
Ph. Eur. 6.2 (Butylhydroxytoluene; Butylated Hydroxytoluene BP 2008). A white or yellowish-white, crystalline powder. F.p. 69° to 70°. Practically insoluble in water; freely soluble in alcohol and in vegetable oils; very soluble in acetone.
USNF 26 (Butylated Hydroxytoluene). A white crystalline solid with a faint characteristic odour. Insoluble in water and in propylene glycol; soluble 1 in 4 of alcohol and 1 in 1.1 of chloroform and of ether.

Incompatibility. Butylated hydroxytoluene is incompatible with oxidising agents and ferric salts. Traces of metals can cause loss of activity.

Adverse Effects
As for Butylated Hydroxyanisole, p.1633.

Effects on the blood. For a report of methaemoglobinaemia associated with the antoxidants (butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate) used to preserve the oil in a soybean infant feed formula, see under Adverse Effects in Alkyl Gallates, p.1628.

Poisoning. A 22-year-old woman experienced severe epigastric cramping, nausea and vomiting, and generalised weakness, followed by dizziness, confusion, and a brief loss of consciousness after ingesting 4 g of butylated hydroxytoluene. She recovered after conservative treatment, which was given 2 days later. The antoxidant had been taken as an unauthorised remedy for genital herpes simplex.[1]

1. Shlian DM, Goldstone J. Toxicity of butylated hydroxytoluene. *N Engl J Med* 1986; **314:** 648–9.

Pharmacokinetics
Butylated hydroxytoluene is readily absorbed from the gastrointestinal tract. It is excreted in the urine mainly as glucuronide conjugates of oxidation products.

Uses
Butylated hydroxytoluene is an antoxidant with uses similar to those of Butylated Hydroxyanisole, p.1633.

Preparations
Proprietary Preparations (details are given in Part 3)
Belg.: Proseptine-Plus.
Multi-ingredient: ***Fr.:*** Cinq sur Cinq.

Cadexomer-Iodine *(BAN)*

Cadexomer Iodine *(USAN)*; Cadexomerjod; Cadexómero yodado; Cadexomerum Iodum; Kadeksomeerijodi. 2-Hydroxymethylene cross-linked (1→4)-α-D-glucan carboxymethyl ether containing iodine.

CAS — 94820-09-4.
ATC — D03AX01.
ATC Vet — QD03AX01.

Adverse Effects and Precautions
As for Povidone-Iodine, p.1659. Some patients have experienced stinging and erythema on application of cadexomer-iodine to their ulcers. Free iodine is released during exposure of cadexomer-iodine preparations to wound exudate and absorption of iodine may occur. Prolonged treatment with cadexomer-iodine should be given with caution in patients with thyroid disorders.

Uses and Administration
Cadexomer-iodine, like povidone-iodine (p.1659), is an iodophore that releases iodine. It is used for its absorbent and antiseptic properties in the management of venous leg ulcers and pressure sores. It is applied as a powder, ointment, or paste containing iodine 0.9%; sufficient powder or ointment should be applied to form a layer about 3 mm thick. Treatment should not usually be continued for more than 3 months.

Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Iodosorb†; ***Austria:*** Iodosorb; ***Canad.:*** Iodosorb; ***Denm.:*** Iodosorb; ***Fin.:*** Iodosorb; ***Fr.:*** Iodosorb†; ***Ger.:*** Iodosorb†; ***Gr.:*** Iodosorb; ***Irl.:*** Iodoflex; ***Ital.:*** Iodosorb; ***Neth.:*** Iodosorb; ***Singapore:*** Iodoflex; Iodosorb; ***Spain:*** Iodosorb†; ***Swed.:*** Iodosorb; ***Switz.:*** Iodosorb; ***UK:*** Iodoflex; Iodosorb.

Calcium Peroxide

Calcium Dioxide; E930.

Пероксид Кальция

CaO_2 = 72.08.

CAS — 1305-79-9;.

Profile
The action of calcium peroxide is similar to that of hydrogen peroxide (p.1647). Calcium peroxide is used in dental products for tooth whitening. It is also used as a flour bleaching and improving agent.

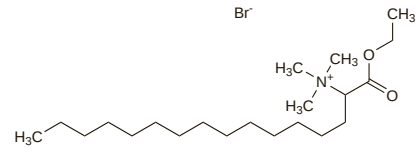
Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** Hexiben.

Carbaethopendecinium Bromide

Carbethopendecinii Bromidum; Carbethoxypentadecyltrimethylammonium Bromide; Karbethopendecinium bromid. 1-Ethoxy-*N*,*N*,*N*-trimethyl-1-oxo-2-hexadecanaminium bromide.

$C_{21}H_{44}NO_2Br$ = 422.5.

CAS — 10567-02-9.



Profile
Carbaethopendecinium bromide is a quaternary ammonium antiseptic with actions and uses similar to those of other cationic surfactants (see Cetrimide, p.1634). It is used in topical preparations for disinfection of skin and mucous membranes.

Preparations
Proprietary Preparations (details are given in Part 3)
Cz.: Mukoseptonex; Ophthalmo-Septonex; Septonex.
Multi-ingredient: ***Cz.:*** Mesocain; Mukoseptonex E; N-Septonex†; Ophthalmo-Septonex; Paradentol†; Septonex; Septonex Plus; Triamcinolon-Ivax.

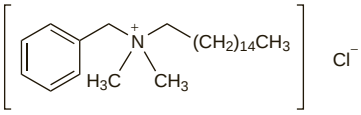
Cetalkonium Chloride *(BAN, USAN, rINN)*

Cetalkonii Chloridum; Cétalkonium, Chlorure de; Cloruro de cetalconio; NSC-32942. Benzylhexadecyldimethylammonium chloride.

Цеталкония Хлорид

$C_{25}H_{46}ClN$ = 396.1.

CAS — 122-18-9.



Profile

Cetalkonium chloride is a quaternary ammonium antiseptic with actions and uses similar to those of other cationic surfactants (see Cetrimide, p.1634). It is used in a variety of topical preparations in the treatment of minor infections of the mouth and throat. It has also been used in the treatment of eye infections. Cetalkonium bromide has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)

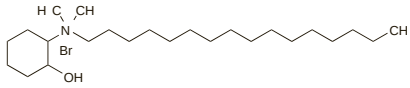
Multi-ingredient: ***Arg.:*** Pansoral; ***Austral.:*** Bonjela; ***Austria:*** Mundisal; ***Braz.:*** Pondicilina; ***Canad.:*** Bionet; ***Cz.:*** Mundisal; ***Fr.:*** Pansoral; ***Ger.:*** Mundisal†; ***Gr.:*** Mundisal; ***Hong Kong:*** Bonjela; ***Hung.:*** Mundisal; ***Irl.:*** Bonjela; ***Israel:*** Baby Gum; Bonjela; ***Malaysia:*** Bonjela; ***NZ:*** Bonjela; ***Pol.:*** Sachol zel Stomatologiczny; ***Rus.:*** Cholisal (Холисал); Pansoral (Пансорал); ***S.Afr.:*** AAA†; Bonjela; ***Singapore:*** Bonjela; ***Switz.:*** Mundisal; Pansoral; Tenderdol; ***Thai.:*** Bonjela; ***UK:*** Bonjela; Bonjela Teething Gel; ***USA:*** Babee.

Cethexonium Bromide

Cetexonio, bromuro de. Hexadecyl(2-hydroxycyclohexyl)dimethylammonium bromide.

$C_{24}H_{50}BrNO$ = 448.6.

CAS — 6810-42-0 (cethexonium); 1794-74-7 (cethexonium bromide); 58703-78-9 (cethexonium chloride).



NOTE. Cethexonium Chloride is *rINN*.

Profile

Cethexonium bromide is a quaternary ammonium antiseptic with properties similar to those of other cationic surfactants (see Cetrimide, p.1634). It is used in preparations for the local treatment of minor infections of the eye, nose, and throat.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Biocidan.

Multi-ingredient: ***Fr.:*** Biocidan.

Cetrimide *(BAN, rINN)*

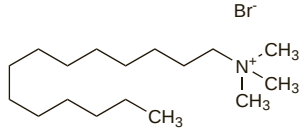
Cetrimid; Cetrimida; Cetrimidas; Cétrimide; Cetrimidum; Cetrymid; Setrimid; Setrimidi.

Цетримид

CAS — 1119-97-7 (trimethyltetradecylammonium bromide); 1119-94-4 (dodecyltrimethylammonium bromide); 8044-71-1 (cetrimide).

ATC — D08AJ04; D11AC01.

ATC Vet — QD08AJ04; QD11AC01.



(trimethyltetradecylammonium bromide)

NOTE. The name cetrimonium bromide was often formerly used for cetrimide. Cetrimonium bromide (see below) is hexadecyltrimethylammonium bromide.

Pharmacopoeias. In *Eur.* (see p.vii) and *Int. Br.* also includes strong cetrimide solution.

Ph. Eur. 6.2 (Cetrimide). It consists of trimethyltetradecylammonium bromide (=tetradonium bromide (*rINN*)) and may contain smaller amounts of dodecyltrimethylammonium bromide and hexadecyltrimethylammonium bromide (=cetrimonium bromide, p.1635). A white or almost white, voluminous, free-flowing powder. Freely soluble in water and in alcohol. A 2.0% solution in water froths copiously when shaken.

BP 2008 (Strong Cetrimide Solution). It is an aqueous solution of cetrimide. It contains 20 to 40% w/v of cetrimide, calculated as $C_{17}H_{38}BrN$ and up to 10% alcohol or isopropyl alcohol, or both; alcohol may be replaced by industrial methylated spirit. It may be perfumed and may contain colouring matter. Store at a temperature above 15°.

Incompatibility. Cetrimide is incompatible with soaps and other anionic surfactants, bentonite, iodine, phenylmercuric nitrate, and alkali hydroxides. Aqueous solutions react with metals.

Adverse Effects and Treatment

At the concentrations used on the skin, solutions of cetrimide and other quaternary compounds do not generally cause irritation, but some patients become hypersensitive to cetrimide after repeated applications. Cetrimide powder is reported to be irritant. There have been rare reports of burns with concentrated solutions of cetrimide.

If ingested, cetrimide and other quaternary ammonium compounds cause nausea and vomiting; strong solutions may cause oesophageal damage and necrosis. They have depolarising muscle relaxant properties and toxic symptoms include dyspnoea and cyanosis due to paralysis of the respiratory muscles, possibly leading to asphyxia. CNS depression (sometimes preceded by excitement and convulsions), hypotension, coma, and death may also occur. Accidental intra-uterine or intravenous administration may cause haemolysis and pulmonary embolism.

Treatment of poisoning is symptomatic; demulcents and diluents may be given if necessary but emesis and lavage should be avoided, particularly if concentrated solutions have been ingested. Activated charcoal may be considered if the patient presents within an hour of ingestion. CNS stimulants and cholinesterase inhibitors are reported not to reverse paralysis due to cetrimide intoxication although sympathomimetics have been tried. Corticosteroids may reduce oropharyngeal oedema.

Effects after cyst irrigation. Adverse effects after irrigation with cetrimide solutions in the treatment of hydatid cysts have included chemical peritonitis,[1] methaemoglobinaemia with cyanosis,[2] and metabolic acidosis.[3]

1. Gilchrist DS. Chemical peritonitis after cetrimide washout in hydatid-cyst surgery. *Lancet* 1979; **ii:** 1374.
2. Baraka A, *et al*. Cetrimide-induced methaemoglobinaemia after surgical excision of hydatid cyst. *Lancet* 1980; **ii:** 88–9.
3. Momblano P, *et al*. Metabolic acidosis induced by cetrimonium bromide. *Lancet* 1984; **ii:** 1045.

Poisoning. The fatal dose of quaternary ammonium compounds was estimated to be 1 to 3 g.[1]

1. Arena JM. Poisonings and other health hazards associated with use of detergents. *JAMA* 1964; **190:** 56–8.

Precautions

Prolonged and repeated applications of cetrimide to the skin are inadvisable as hypersensitivity may occur. Contact with the eyes, brain, meninges, and middle ear should be avoided. Cetrimide is for external use only and should not be used in body cavities or as an enema.

Quaternary ammonium compounds are not reliable for sterilising surgical instruments and heat-labile articles. The antimicrobial activity of quaternary ammonium compounds may be reduced through absorption, or through combination with organic matter, or by reducing pH.

Solutions of quaternary ammonium compounds should not be used for disinfection of soft contact lenses.

Aqueous solutions of cetrimide or other quaternary ammonium disinfectants may be susceptible to contamination with micro-organisms. To reduce this risk, a sterilised preparation should be used or, where necessary, solutions must be freshly prepared at the recommended concentration and appropriate measures should be taken to prevent contamination during storage or dilution.

Handling. Cetrimide powder is irritant; it has been recommended that the nose and mouth should be protected by a mask when working with the powder[1] and eyes should be protected by goggles.

1. Jacobs JY. Work hazards from drug handling. *Pharm J* 1984; **233:** 195–6.

Uses and Administration

Cetrimide is a quaternary ammonium antiseptic with actions and uses typical of cationic surfactants. These surfactants dissociate in aqueous solution into a relatively large and complex cation that is responsible for the surface activity and a smaller inactive anion. In addition to emulsifying and detergent properties, quaternary ammonium compounds have bactericidal activity against Gram-positive and, at a higher concentration, against some Gram-negative bacteria. Some *Pseudomonas* spp. are particularly resistant as are strains of *Mycobacterium tuberculosis*. They are ineffective against bacterial spores, have variable antifungal activity, and are effective against some viruses.

Quaternary ammonium compounds are most effective in neutral or slightly alkaline solution and their bactericidal activity is appreciably reduced in acid media; their activity is enhanced by alcohols.

Like other quaternary ammonium compounds, notably benzalkonium chloride (p.1629), cetrimide has been employed for cleansing skin, wounds (but see under Wound Disinfection, p.1624), and burns. For these purposes it has been used as a 0.1 to 1.0% aqueous solution, generally prepared by dilution of a more concentrated solution, or as a cream or spray containing 0.5%. However, a mixture of cetrimide with chlorhexidine (p.1635) has often been preferred to cetrimide alone. This combination is also used in a lotion for acne (p.1577).

Solutions containing up to 10% of cetrimide have been used as shampoos to remove the scales in seborrhoeic dermatitis (p.1584).

Cetrimide solution 0.5 or 1% has been used as a scolicide to irrigate hydatid cysts during surgery (see Echinococcosis, p.136) but systemic adverse effects have been reported (see above).

Cetrimide and benzalkonium chloride are also used as preservatives in cosmetics and pharmaceutical formulations including eye drops and in disinfecting solutions for hard contact lenses; neither compound should be used for disinfection of soft contact lenses.

Cetrimide is also present in some emulsifying preparations such as Cetrimide Emulsifying Ointment (BP 2008).

Preparations

BP 2008: Cetrimide Cream; Cetrimide Emulsifying Ointment; Cetrimide Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Boucren; Sorbicet; ***Fr.:*** Cetavlon; Sterilene; ***Gr.:*** Cetavlon; ***Irl.:*** Cetavlex†; Vesagex; ***Malaysia:*** Cetavlex†; Dermoplex Antiseptic; ***Port.:*** Cetavlex; ***Singapore:*** Acnederm Wash; ***Spain:*** Cetavlon†; ***Turk.:*** Cetyl; ***UK:*** Bansor†; Cetavlex; Medi-Prep; Medicaid; Richmond Antiseptic Cream; Vesagex.

Multi-ingredient: ***Arg.:*** Cerosporin GS†; Jabonacid; Otidrops; Otocalmia Biotic; Sincerum; ***Austral.:*** Acnederm Foaming Wash; Curacleanse†; Dimethicream; Hamilton Pine Tar with Menthol; Hamilton Skin Repair†; Medi Creme; Microshield Antiseptic; Pro-PS†; Savlon Antiseptic; Soov Bite; Soov Burn; Soov Cream; ***Austria:*** Lemocin; Xylonor; ***Belg.:*** Lemocin; ***Braz.:*** Cetrilan; ***Canad.:*** Savlodil; ***Cz.:*** Hibicet Hospital Concentrate†; ***Fr.:*** Broncorinol rhinites†; Lysocalmspray; Rectoquotane; ***Gr.:*** Hibicet; ***Hong Kong:*** Acnederm Wash; B-Gel; Borraginol-N; Drapolene†; Hamilton Skin Repair; Hibicet Hospital Concentrate†; Medicreme; Soov Bite; Soov Cream; Tri-Gel; Zinsomine; ***India:*** Iteol-3; Scabine; Scarab; Siloderm; ***Indon.:*** Benzomid; Bioacne; Borraginol-N; Borraginol-S; Neo Resiguard; Pravlon; ***Irl.:*** Ceanel†; Drapolene; Hibicet; RBC; Savlon; Siopel†; Torbetol; ***Israel:*** Cetrin; Savior; Septacare†; Tisept; Travasept; ***Ital.:*** Baxidin; Cetrexidin; Cetrisan; Clotramid†; Cuprosodio; Farvicett; Hibizene; Lidocaina Spray; Panseptil; Steridol†; ***Malaysia:*** Acnederm Foaming Wash; Burnol Plus; Drapolene; Hibicet†; Soov Bite; ***Neth.:*** Hibicet concentraat; Hibicet verdunning; ***NZ:*** Acnederm Foaming Wash; Acnederm Wash†; Hairscience Conditioner†; Karicare Barrier Cream†; Medicreme; Savlon; Soov Bite; Soov Burn; Soov Cream; Soov Gel; ***Philipp.:*** Drapolene; ***Rus.:*** Drapolene (Драполен); ***S.Afr.:*** Benzet†; Germolene; Hibicet†; Medituss†; Siopel; Trochain; Virobis†; ***Singapore:*** Burnol Plus; Drapolene; Napitol†; Savlon†; Soov Bite; Soov Cream; ***Switz.:*** Gem; ***Thai.:*** Bacard; Burnol Plus; Chlorhex-C; Dekka; Drapolene; Frebac; Hibicet†; Inhibac; Napilene; Sepdine†; Septone†; ***Turk.:*** Drapolene; Savlex; Savonol; Savrolin; Setilin; ***UK:*** Ceanel; Cetanorm; Cymex; Dermidex; Drapolene; Hibicet†; Lypsyl Cold Sore Gel; Neo Baby Cream; Quinoderm Antibacterial Face Wash; Savlon Antiseptic Cream; Savlon Antiseptic Liquid; Siopel; Steripod Chlorhexidine Gluconate with Cetrimide†; Tisept; Torbetol; Travasept; ***USA:*** Scadan.