

**Docusate Sodium** (BAN, USAN, rINN)

Diocetyl Sodium Sulfosuccinate; Diocetyl Sodium Sulphosuccinate; Docusate sodique; Docusato de sodio; Docusato sódico; Docusatum Natrium; Dokusaatinatrium; Dokusát sodná sůl; Dokusatnatrium; Dokuzát-nátrium; Dokuzato natrio druska; DSS; Natrii docusas; Sodium Diocetyl Sulphosuccinate; Soda dokuzynin. Sodium 1,4-bis(2-ethylhexyl) sulphosuccinate.

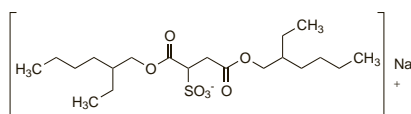
Докузат Натрий

$C_{20}H_{37}NaO_5S = 444.6$ .

CAS — 577-11-7.

ATC — A06AA02.

ATC Vet — QA06AA02.



NOTE: Compounded preparations of docusate sodium may be represented by the following names:

- Co-danthrusate (BAN)—docusate sodium 6 parts and dantron 5 parts.

**Pharmacopoeias.** In *Eur.* (see p.vii) and *US*.

**Ph. Eur. 6.2** (Docusate Sodium). White or almost white, hygroscopic, waxy masses or flakes. Sparingly soluble in water; freely soluble in alcohol and in dichloromethane. Store in airtight containers.

**USP 31** (Docusate Sodium). A white wax-like plastic solid with a characteristic odour suggestive of octyl alcohol. Slowly soluble 1 in 70 of water; freely soluble in alcohol and in glycerol; very soluble in petroleum spirit.

**Adverse Effects and Precautions**

Adverse effects occur rarely with docusates; diarrhoea, nausea, abdominal cramps, and skin rash have been reported. Anorectal pain or bleeding have occasionally occurred after rectal doses.

Like all laxatives, docusates should not be used when intestinal obstruction or undiagnosed abdominal symptoms are present; prolonged use should be avoided. Docusate sodium should not be given rectally to patients with haemorrhoids or anal fissures.

Docusate sodium should not be used to soften ear wax when the ear is inflamed or the ear drum perforated.

**Hypersensitivity.** Docusate salts are widely used as anionic surfactants in pharmaceutical formulations. Allergic contact dermatitis has been reported from one such preparation; patch testing confirmed the reaction to docusate sodium.<sup>1</sup>

1. Lee A-Y, Lee K-H. Allergic contact dermatitis from dioctyl sodium sulfosuccinate in a topical corticosteroid. *Contact Dermatitis* 1998; **38**: 355-6.

**Pregnancy.** Hypomagnesaemia in a neonate, manifested by jitteriness, was considered to be secondary to maternal hypomagnesaemia caused by maternal use of docusate sodium during pregnancy.<sup>1</sup>

1. Schindler AM. Isolated neonatal hypomagnesaemia associated with maternal overuse of stool softener. *Lancet* 1984; **ii**: 822.

**Interactions**

Docusates may enhance the gastrointestinal uptake of other drugs, such as liquid paraffin (and the two should not be given together). Dosage of anthraquinone laxatives may need to be reduced if used with docusates. It has also been suggested that giving docusates with aspirin increases the incidence of adverse effects on the gastrointestinal mucosa.

**Pharmacokinetics**

Docusate salts are absorbed from the gastrointestinal tract and excreted in bile. Docusate sodium is also distributed into breast milk.

**Uses and Administration**

Docusates are given as the calcium or sodium salt and are used as laxatives in the management of constipation (p.1693) or to reduce straining in patients with haemorrhoids (p.1697) or anal fissure. They are also used as adjuncts for bowel evacuation before abdominal radiological procedures. Docusate potassium has also been used.

The symbol † denotes a preparation no longer actively marketed

Docusates are anionic surfactants which have been considered to act primarily by increasing the penetration of fluid into the faeces, but may also have other effects on intestinal fluid secretion, and probably act both as stimulants and as faecal softening agents.

The usual daily oral dose of docusate calcium is 240 mg. Docusate sodium is given in usual oral doses of 50 to 300 mg daily in divided doses, although doses of up to 500 mg daily may be used. (For administration in children, see below). The effect is usually seen within 12 to 72 hours. When used as an adjunct to abdominal radiological procedures, an oral dose of 400 mg is given with the barium meal. It is also given rectally as an enema in doses of 120 mg; the effect is usually seen in 5 to 20 minutes. Docusate sodium is also used with anthraquinone stimulant laxatives such as casanthranol (p.1715), dantron (p.1722), and senna (p.1769).

Docusate sodium is used for softening wax in the ear as ear drops containing 0.5 or 5%.

Docusate sodium and other docusate salts are widely used as anionic surfactants in pharmaceutical formulations.

**Administration in children.** Docusate sodium by mouth is licensed in the UK for the treatment of chronic constipation in children aged 6 months and over. More specific dose details are also provided in the *BNFC* as follows:

- 6 months to 2 years: 12.5 mg three times daily
- 2 to 12 years: 12.5 to 25 mg three times daily

Children aged 12 years and over may be given the adult doses for constipation, either orally or rectally (see Uses and Administration, above). Adult formulations are not licensed for use in children under 12 years.

In the USA, children aged 2 to 12 years may be given docusate sodium in doses of 50 to 150 mg daily, either as a single daily dose or in divided doses. Docusate calcium is generally only used in the USA for children aged 12 years and over.

Docusate sodium is also used as an **adjunct in abdominal radiological procedures**. UK licensed product information suggests that children may be given an oral dose of 75 mg (30 mL of docusate sodium paediatric solution 12.5 mg per 5 mL) with the barium meal. The *BNFC* recommends that those aged 12 years and over are given the usual adult dose (see above).

**Ear wax removal.** Cerumen or ear wax is a normal secretion of the ceruminous glands present in the lining of the external auditory canal. Excessive accumulation or impaction of ear wax may decrease hearing acuity, and may also produce dizziness, vertigo, reflex coughing, tinnitus, and otalgia.

Syringing of the external auditory canal with warm water may be used to remove wax from the ear. However, complications include pain, perforation of the ear drum, deafness, dizziness, vertigo, tinnitus, and infection.<sup>1-6</sup> Contra-indications to ear syringing include past perforation, ear infection, previous ear surgery; syringing may be difficult in children.<sup>1,6</sup>

A ceruminolytic agent may be given as ear drops to soften, loosen, or dissolve cerumen instead. They may also be used immediately before syringing, or for several days beforehand.<sup>1-3,5,6</sup> Traditionally, fixed oils such as arachis oil, olive oil, or almond oil have been used.<sup>1</sup> Some still advocate the use of olive oil to reduce the recurrence of impacted cerumen,<sup>3</sup> while others consider it to be ineffective.<sup>5</sup> Other ceruminolytics that have been reported as effective include docusates,<sup>4,7,8</sup> peroxides such as hydrogen peroxide or urea hydrogen peroxide,<sup>4,9</sup> and trolamine polypeptide oleate-condensate,<sup>4,8</sup> although some studies have found these to be no more effective in removing wax than a saline control.<sup>10,11</sup> Other agents that have been used include acetic acid,<sup>4</sup> choline salicylate,<sup>12</sup> methyltrypsin solution,<sup>5</sup> and an oily solution of paradichlorobenzene and chlorobutanol.<sup>4,12</sup> Glycerol and sodium bicarbonate solution have also been used. However, a comparative study *in vitro* of the efficacy of various wax dispersing agents found the most effective to be water, which had originally been included as a control,<sup>13</sup> and a systematic review<sup>14</sup> concluded that saline or water ear drops seemed to be as good as proprietary agents for the removal of ear wax, although there was a lack of good quality studies on which to base recommendations.

Ear candling is a traditional folk remedy that has been used to remove cerumen, but studies indicate it is ineffective, and may deposit wax in the ear canal or cause burn injuries.<sup>3,4</sup>

1. Sharp JF, *et al.* Ear wax removal: a survey of current practice. *BMJ* 1990; **301**: 1251-3.
2. Grossan M. Cerumen removal—current challenges. *Ear Nose Throat J* 1998; **77**: 541-6, 548.
3. Grossan M. Safe, effective techniques for cerumen removal. *Geriatrics* 2000; **55**: 80, 83-6.
4. Dimmitt P. Cerumen removal products. *J Pediatr Health Care* 2005; **19**: 332-6.
5. Midani A, *et al.* Safety and efficacy of Sofenz ceruminolytic solution. *Ear Nose Throat J* 2006; **85**: 87-8, 90-2.
6. Aung T, Mulley GP. Removal of ear wax. *BMJ* 2002; **325**: 27.
7. Chen DA, Caparosa RJ. A nonprescription ceruminolytic. *Am J Otol* 1991; **12**: 475-6.

8. Singer AJ, *et al.* Ceruminolytic effects of docusate sodium: a randomized, controlled trial. *Ann Emerg Med* 2000; **36**: 228-32.
9. Fahmey S, Whitefield M. Multicentre clinical trial of Exterol as a cerumenolytic. *Br J Clin Pract* 1982; **36**: 197-204.
10. Whitley VN, *et al.* Randomized clinical trial of docusate, triethanolamine polypeptide, and irrigation in cerumen removal in children. *Arch Pediatr Adolesc Med* 2003; **157**: 1177-80.
11. Roland PS, *et al.* Randomized, placebo-controlled evaluation of Cerumenex and Murine earwax removal products. *Arch Otolaryngol Head Neck Surg* 2004; **130**: 1175-7.
12. Dummer DS, *et al.* A single-blind, randomized study to compare the efficacy of two ear drop preparations ('Audaux' and 'Cerumol') in the softening of ear wax. *Curr Med Res Opin* 1992; **13**: 26-30.
13. Andaz C, Whittet HB. An *in vitro* study to determine efficacy of different wax-dispersing agents. *ORL J Otorhinolaryngol Relat Spec* 1993; **55**: 97-9.
14. Burton MJ, Dorée CJ. Ear drops for the removal of ear wax. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2003 (accessed 13/11/06).

**Preparations**

**BP 2008:** Co-danthrusate Capsules; Compound Docusate Enema; Docusate Capsules; Docusate Oral Solution; Paediatric Docusate Oral Solution; **USP 31:** Docusate Calcium Capsules; Docusate Potassium Capsules; Docusate Sodium Capsules; Docusate Sodium Solution; Docusate Sodium Syrup; Docusate Sodium Tablets; Ferrous Fumarate and Docusate Sodium Extended-release Tablets.

**Proprietary Preparations** (details are given in Part 3)

**Arg.:** Cerumex; Otcoclean Solucion de Limpieza; Phillips; **Austral.:** Coloxyl; Rectalad; Vaxsol; **Belg.:** Norgalax; **Canad.:** Calax; Colace; Cor-rectol Stool Softener; Ex-Lax Stool Softener; Regulex; Selax; Silace; Sof-lax; Surfak; **Chile:** Regal; **Fr.:** Jarmylene; Norgalax; **Ger.:** Ottex; Ottowaxol; **Hong Kong:** Norgalax; Vaxsol; **India:** Desol; Laxicon; **Indon.:** Forumen; Vaxsol; **Irl.:** Norgalax; **Malaysia:** Solu-wax; Vaxsol; **Mex.:** Correctol; **Neth.:** Norgalax; **NZ:** Coloxyl; Vaxsol; **Philipp.:** Otosol; **Pol.:** Laxol; Laxopol; **Port.:** Norgalax; **S.Afr.:** Vaxsol NF; **Singapore:** Norgalax; Solu-wax; Vaxsol; **Spain:** Dama-Lax; **Switz.:** Norgalax; **Thai.:** Cusate; Dewax; Vaxsol; **UK:** Clear Ear; Diocetyl; Docusol; DulcoEase; Fletchers Enemette; Molcer; Norgalax; Vaxsol; **USA:** Colace; D-S-S; DC Softgels; DOK; Docusoft; DOK; DOS Softgel; Dulcolax Stool Softener; Ex-Lax Stool Softener; Regulax; SS; Silace; Sof-lax; Surfak; Surfak.

**Multi-ingredient Arg.:** Candilax; Nigalax; **Austral.:** Chemists Own Natural Laxative with Softener; Coloxyl; Coloxyl with Senna; Comblax; Sennosoft; Soflax; **Austria:** Purigoat; **Yal. Belg.:** Laxavit; Softene; **Braz.:** Ventre Livre; **Canad.:** Fruitatves; Gentilax; S; Peri-Colace; Senna-S; Senokot-S; **Cz.:** Yal; **Denm.:** Analga; Glyokyl; **Klyx. Fin.:** Klyx; **Fr.:** Doculys; **Ger.:** Norgalax; Miniklistier; **Yal. Gr.:** Florisan; **Hung.:** Yal; **India:** Hepasul; Purenid-Int; **Israel:** Migraleve; **Ital.:** Macrolax; Sorbicid; **Mex.:** Clys-Go; **Neth.:** Klyx; **Norw.:** Klyx; **NZ:** Coloxyl; Coloxyl with Senna; Laxsol; **Port.:** Clys-Go; **Spain:** Boldolaxin; Laxvit; Migraleve; **Swed.:** Emulax; Klyx; **Switz.:** Klyx; Magnum; **Yal. Thai.:** Bisolax; Hemorhin; **UK:** Capsuvac; Normax; **USA:** Docusoft; Plus; Doxidant; Dulcolax Bowel Prep Kit; Ex-Lax Gentle Strength; Genasoft Plus Softgels; Laxative & Stool Softener; Nu-Natal Advanced; Peri-Colace; Peri-Dos Softgels; Senna Plus; Senna-S; Senokot-S; Silace-C; Therevac Plus; Therevac SB; X-Prep Bowel Evacuant Kit-I; **Ven. ez.:** Clys-Go; Senokot con Docusate.

Used as an adjunct in **India:** Softenon; Softenon-Z; **Indon.:** Fercee; Viliron; **Philipp.:** TriHEMIC; **USA:** Anemagen OB; Citracal Prenatal; Citracal Prenatal + DHA; Ferro-Dok; Hem Fe; Hemaspant; Natal Extra; Nephron FA; Obstetrix; Optinate Omega-3; Prenatal; TriHEMIC; Vinate GT.

**Dolasetron Mesilate** (BANM, rINN/M)

Dolasetron, Mésilate de; Dolasetron Mesilate (USAN); Dolasetroni Mesilas; MDL-73147EF (dolasetron or dolasetron mesilate); Mesilato de dolasetron. (6R,8r,9aS)-3-Oxopropylhydro-2H-2,6-methanoquinolizin-8-yl indole-3-carboxylate methanesulphonate.

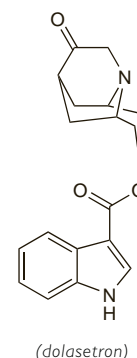
Доласетрона Мезилат

$C_{19}H_{20}N_2O_3 \cdot CH_4O_3S = 420.5$ .

CAS — 115956-12-2 (dolasetron); 115956-13-3 (dolasetron mesilate).

ATC — A04AA04.

ATC Vet — QA04AA04.



(dolasetron)

**Pharmacopoeias.** In *US*.

**USP 31** (Dolasetron Mesilate). A white to off-white powder. Freely soluble in water and in propylene glycol; slightly soluble in alcohol and in sodium chloride 0.9%. Protect from light.

**Stability.** A study<sup>1</sup> of the stability of two extemporaneous oral suspensions of dolasetron mesilate 10 mg/mL prepared from