Docusate Sodium *(BAN, USAN, rINN)*

Dioctyl Sodium Sulfosuccinate; Dioctyl Sodium Sulphosuccinate; Docusate sodique; Docusato de sodio; Docusato sódico; Docusatum Natricum; Dokusaattinatrium; Dokusát sodná sůl; Dokusatnatrium; Dokuzát-nátrium; Dokuzato natrio druska; DSS; Natrii docusas; Sodium Dioctyl Sulphosuccinate; Sodu dokuzynian. Sodium 1,4-bis(2-ethylhexyl) sulphosuccinate.

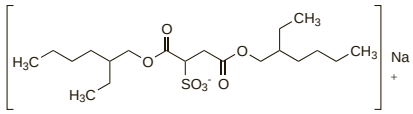
Докузат Натрий

$C_{20}H_{37}NaO_7S$ = 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 octil 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.[1]

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.[1]

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.

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.[1-6] Contra-indications to ear syringing include past perforation, ear infection, previous ear surgery; syringing may be difficult in children.[1,6]

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.[1-3,5,6] Traditionally, fixed oils such as arachis oil, olive oil, or almond oil have been used.[1] Some still advocate the use of olive oil to reduce the recurrence of impacted cerumen,[3] while others consider it to be ineffective.[5] Other ceruminolytics that have been reported as effective include docusates,[4,7,8] peroxides such as hydrogen peroxide or urea hydrogen peroxide,[4,9] and trolamine polypeptide oleate-condensate,[4,8] although some studies have found these to be no more effective in removing wax than a saline control.[10,11] Other agents that have been used include acetic acid,[4] choline salicylate,[12] methyltrypsin solution,[5] and an oily solution of paradichlorobenzene and chlorobutanol.[4,12] 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,[13] and a systematic review[14] 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.[3,4]

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 cerumenolytic. *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. Whatley 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 ('Audax' 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; Otoclean Solucion de Limpieza†; Phillips†; ***Austral.:*** Coloxyl; Rectalad; Waxsol; ***Belg.:*** Norgalax; ***Canad.:*** Calax; Colace; Correctol Stool Softener; Ex-Lax Stool Softener†; Regulex†; Selax; Silace; Soflax; Surfak†; ***Chile:*** Regal†; ***Fr.:*** Jamylene; Norgalax†; ***Ger.:*** Otitex; Otowaxol; ***Hong Kong:*** Norgalax†; Waxsol; ***India:*** Desol; Laxicon; ***Indon.:*** Forumen; Waxsol; ***Irl.:*** Norgalax†; Waxsol; ***Malaysia:*** Soluwax; Waxsol†; ***Mex.:*** Correctol†; ***Neth.:*** Norgalax; ***NZ:*** Coloxyl; Waxsol; ***Philipp.:*** Otosol; ***Pol.:*** Laxol; Laxopol; ***Port.:*** Norgalax; ***S.Afr.:*** Waxsol NF; ***Singapore:*** Norgalax†; Soluwax; Waxsol; ***Spain:*** Dama-Lax†; ***Switz.:*** Norgalax; ***Thai.:*** Cusate; Dewax; Waxsol; ***UK:*** Clear Ear; Dioctyl; Docusol; DulcoEase; Fletchers Enemette†; Molcer; Norgalax; Waxsol; ***USA:*** Colace; D-S-S; DC Softgels; Dioctyn; Docusoft; DOK; DOS Softgel; Dulcolax Stool Softener; Ex-Lax Stool Softener; Regulax SS; Silace; Sof-lax; Sulfolax; Surfak.

Multi-ingredient: ***Arg.:*** Candilax; Nigalax; ***Austral.:*** Chemists Own Natural Laxative with Softener; Coloxyl; Coloxyl with Senna; Combilax; Sennesoft; Soflax; ***Austria:*** Purigoa†; Yal; ***Belg.:*** Laxavit; Softene; ***Braz.:*** Ventre Livre†; ***Canad.:*** Fruitatives†; Gentlax S; Peri-Colace†; Senna-S; Senokot-S; ***Cz.:*** Yal; ***Denm.:*** Analka; Glyoktyl; Klyx; ***Fin.:*** Klyx; ***Fr.:*** Doculyse; ***Ger.:*** Norgalax Miniklistier; Yal; ***Gr.:*** Florisan; ***Hung.:*** Yal†; ***India:*** Hepasules; Pursennid-In†; ***Israel:*** Migraleve; ***Ital.:*** Macrolax; Sorbiclis; ***Mex.:*** Clyss-Go; ***Neth.:*** Klyx; ***Norw.:*** Klyx; ***NZ:*** Coloxyl; Coloxyl with Senna; Laxsol; ***Port.:*** Clyss-Go; ***Spain:*** Boldolaxin†; Laxvital; Migraleve; ***Swed.:*** Emulax; Klyx; ***Switz.:*** Klyx Magnum; Yal; ***Thai.:*** Bisolax; Hemorhin; ***UK:*** Capsuvac; Normax; ***USA:*** Docusoft Plus; Doxidan†; 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-1; ***Venez.:*** Clys-Go†; Senokot con Docusato.

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

Dolasetron Mesilate *(BANM, rINNM)*

Dolasétron, Mésilate de; Dolasetron Mesylate *(USAN)*; Dolasetroni Mesilas; MDL-73147EF (dolasetron or dolasetron mesilate); Mesilato de dolasetrón. (6*R*,8*r*,9a*S*)-3-Oxoperhydro-2*H*-2,6-methanoquinolizin-8-yl indole-3-carboxylate methanesulphonate.

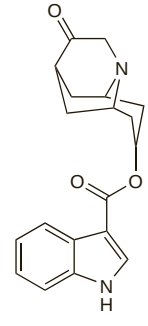
Доласетрона Мезилат

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

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

ATC — A04AA04.

ATC Vet — QA04AA04.



(dolasetron)

Pharmacopoeias. In *US*.

USP 31 (Dolasetron Mesylate). 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[1] of the stability of two extemporaneous oral suspensions of dolasetron mesilate 10 mg/mL prepared from

commercially available tablets found them to be stable for at least 90 days when stored at 3 to 5° and at 23 to 25°.

1. Johnson CE, *et al.* Stability of dolasetron in two oral liquid vehicles. *Am J Health-Syst Pharm* 2003; **60:** 2242–4.

Adverse Effects and Precautions

As for Ondansetron, p.1757. Diarrhoea, anorexia, and abdominal pain may also occur. Various ECG changes have been noted with dolasetron. Dolasetron should be used with caution in patients who have, or may develop, prolongation of the QT interval or other alterations in cardiac conduction intervals, and in those with electrolyte imbalances. Other adverse effects include dyspepsia, flatulence, taste disturbances, fever, chills or shivering, sleep disorders, fatigue, and drowsiness. There have been rare reports of intestinal obstruction, pancreatitis, jaundice, seizures, bronchospasm, cardiac arrhythmias, and oedema. Local reactions may occur on intravenous use. No dosage reduction is considered necessary in renal or hepatic impairment, despite possible reductions in clearance.

Effects on the cardiovascular system. For a discussion of the effects of 5-HT_3 antagonists on the cardiovascular system, see under Ondansetron, p.1757.

Phlebitis. Venous irritation has been reported after intravenous use of dolasetron; diluting subsequent doses with sodium chloride 0.9% and infusing it more slowly markedly reduced the frequency of phlebitis.[1]

1. Oshiro MM. Dolasetron-associated venous irritation. *Am J Health-Syst Pharm* 2000; **57:** 1533–4.

Interactions

Plasma concentrations of hydrodolasetron, the active metabolite of dolasetron, are increased by cimetidine and atenolol and decreased by rifampicin. Dolasetron should be used with caution in patients taking drugs that prolong the QT interval, including those likely to cause electrolyte disturbances (see also p.1757).

Pharmacokinetics

Dolasetron given orally or intravenously is rapidly converted to the active metabolite hydrodolasetron by carbonyl reductase, a ubiquitous enzyme. Peak plasma concentrations of hydrodolasetron occur 1 hour after oral, and 0.6 hours after intravenous, doses of dolasetron. The apparent oral bioavailability of dolasetron determined as hydrodolasetron is about 75%. It has a mean elimination half-life of about 7 to 8 hours.

Hydrodolasetron is partially metabolised by the cytochrome P450 isoenzymes CYP2D6 and CYP3A and about 50 to 60% is eliminated unchanged in the urine. Two thirds of a dose of dolasetron is recovered in the urine and one third in the faeces.

Clearance of hydrodolasetron is increased in children, but is not altered in the elderly. Clearance is reduced in severe hepatic impairment (Child-Pugh category B or C) and in severe renal impairment (creatinine clearance less than 10 mL/min) after oral use. After intravenous use, clearance is reduced in severe renal impairment but apparently unchanged in severe hepatic impairment.

◊ References.

1. Lerman J, *et al.* Pharmacokinetics of the active metabolite (MDL 74,156) of dolasetron mesylate after oral or intravenous administration to anesthetized children. *Clin Pharmacol Ther* 1996; **60:** 485–92.
2. Dempsey E, *et al.* Pharmacokinetics of single intravenous and oral doses of dolasetron mesylate in healthy elderly volunteers. *J Clin Pharmacol* 1996; **36:** 903–10.
3. Stubbs K, *et al.* Pharmacokinetics of dolasetron after oral and intravenous administration of dolasetron mesylate in healthy volunteers and patients with hepatic dysfunction. *J Clin Pharmacol* 1997; **37:** 926–36.
4. Dimmitt DC, *et al.* Pharmacokinetics of oral and intravenous dolasetron mesylate in patients with renal impairment. *J Clin Pharmacol* 1998; **38:** 798–806.
5. Dimmitt DC, *et al.* Effect of infusion rate on the pharmacokinetics and tolerance of intravenous dolasetron mesylate. *Ann Pharmacother* 1998; **32:** 39–44.

Uses and Administration

Dolasetron is a 5-HT_3 antagonist with antiemetic actions similar to those of ondansetron (see p.1757). It is used as the mesilate in the prevention of nausea and vomiting (p.1700) associated with chemotherapy, and in the prevention and treatment of postoperative nausea and vomiting.

For *prevention* of acute **nausea and vomiting** associated with **chemotherapy** dolasetron mesilate may be given orally in a dose of 100 mg (in the USA) or 200 mg (in most other countries including the UK) within 1 hour before treatment. Alternatively, it may be given in a dose of 1.8 mg/kg, or 100 mg, by intravenous injection at a rate of up to 100 mg over 30 seconds about 30 minutes before chemotherapy; the same dose may be diluted to 50 mL with a suitable infusion solution and given intravenously over up to 15 minutes. To protect against delayed emesis, a further 200-mg dose may be given orally once daily; in Europe and the UK dolasetron may not normally be given for more than 4 consecutive days per chemotherapy cycle although some countries permit use for up to 7 days.

When given for the *prevention* of **postoperative** nausea and vomiting the recommended dose is usually 50 mg of dolasetron mesilate orally before induction of anaesthesia or 12.5 mg intravenously at the end of anaesthesia. In the USA, it is given as a 100-mg oral dose within 2 hours before surgery, or 12.5 mg intravenously about 15 minutes before the end of anaesthesia. The same intravenous dose may be given for the *treatment* of postoperative nausea and vomiting.

The use of dolasetron mesilate in **children** is licensed in some countries, including the USA. However, others have not licensed such use and in the UK it is contraindicated in children and adolescents under 18 years of age because they may be at increased risk of acute changes in the QT interval, and there have been reports of cardiac conduction disorders, cardiac arrest, and myocardial infarction in children treated with dolasetron. In the USA, children over 2 years of age may be given dolasetron mesilate 1.8 mg/kg orally (within 1 hour before chemotherapy) or intravenously (about 30 minutes before chemotherapy), up to a maximum dose of 100 mg, to prevent acute chemotherapy-induced nausea and vomiting. For prevention of postoperative nausea and vomiting, 1.2 mg/kg by mouth, up to a maximum of 100 mg, may be given within 2 hours before surgery; or 350 micrograms/kg, up to a maximum of 12.5 mg, may be given intravenously 15 minutes before the end of anaesthesia. The same intravenous dose may be given to treat established postoperative nausea and vomiting.

◊ Reviews.

1. Balfour JA, Goa KL. Dolasetron: a review of its pharmacology and therapeutic potential in the management of nausea and vomiting induced by chemotherapy, radiotherapy or surgery. *Drugs* 1997; **54:** 273–98.
2. Anonymous. Dolasetron for prevention of nausea and vomiting due to cancer chemotherapy. *Med Lett Drug Ther* 1998; **40:** 53–4.

Pruritus. Dolasetron and other 5-HT_3 antagonists have been investigated for the management of pruritus (see under Ondansetron, p.1758).

Preparations

USP 31: Dolasetron Mesylate Injection; Dolasetron Mesylate Oral Solution; Dolasetron Mesylate Oral Suspension; Dolasetron Mesylate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Anzemet†; ***Austral.:*** Anzemet; ***Austria:*** Anzemet; ***Braz.:*** Anzemet; ***Canad.:*** Anzemet; ***Cz.:*** Anzemet†; ***Fin.:*** Anzemet†; ***Fr.:*** Anzemet; ***Ger.:*** Anemet; ***Gr.:*** Anzemet; ***Hung.:*** Anemet†; ***Ital.:*** Anzemet; ***Mex.:*** Anzemet; ***Neth.:*** Anzemet; ***S.Afr.:*** Zamanon; ***Switz.:*** Anzemet; ***UK:*** Anzemet; ***USA:*** Anzemet; ***Venez.:*** Anzemet.

Domperidone *(BAN, USAN, rINN)*

Domperidon; Domperidona; Domperidonas; Dompéridone; Domperidoni; Domperidonum; R-33812. 5-Chloro-1-{1-[3-(2-oxobenzimidazolin-1-yl)propyl]-4-piperidyl}benzimidazolin-2-one.

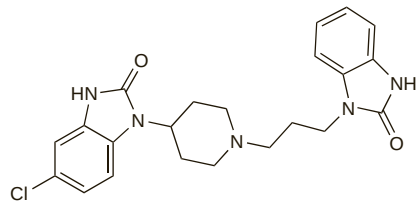
Домперидон

$C_{22}H_{24}ClN_5O_2$ = 425.9.

CAS — 57808-66-9.

ATC — A03FA03.

ATC Vet — QA03FA03.



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

Ph. Eur. 6.2 (Domperidone). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol and in methyl alcohol; soluble in dimethylformamide. Protect from light.

Domperidone Maleate *(BANM, rINNM)*

Dompéridone, maléate de; Domperidoni maleas; Domperidon-imaleaatti; Domperidonmaleat; Domperidon-maleát; Domperidon-maleinát; Domperidono maleatas; Maleato de domperidona.

Домперидона Малеат

$C_{22}H_{24}ClN_5O_2.C_4H_4O_4$ = 542.0.

CAS — 99497-03-7.

ATC — A03FA03.

ATC Vet — QA03FA03.

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

Ph. Eur. 6.2 (Domperidone Maleate). A white or almost white powder; it exhibits polymorphism. Very slightly soluble in water and in alcohol; sparingly soluble in dimethylformamide; slightly soluble in methyl alcohol. Protect from light.

Adverse Effects

Plasma-prolactin concentrations may be increased, which may lead to galactorrhoea or gynaecomastia. There have been reports of reduced libido, and rashes and other allergic reactions. Domperidone does not readily cross the blood-brain barrier and the incidence of central effects such as extrapyramidal reactions or drowsiness may be lower than with metoclopramide (p.1748); however, there have been reports of dystonic reactions.

Domperidone by injection has been associated with convulsions, arrhythmias, and cardiac arrest. Fatalities have restricted use by this route.

Effects on the cardiovascular system. Sudden death has occurred in cancer patients given domperidone *intravenously* in high doses.[1-3] Four cancer patients experienced cardiac arrest after high intravenous doses[4] and 2 of 4 similar patients had ventricular arrhythmias.[5] After such reports the injection has been withdrawn from general use in many countries, including the UK.

Prolongation of the QT interval has been reported in an infant given *oral* domperidone, with normalisation after the drug was stopped.[6]

1. Joss RA, *et al.* Sudden death in cancer patient on high-dose domperidone. *Lancet* 1982; **i:** 1019.
2. Giaccone G, *et al.* Two sudden deaths during prophylactic antiemetic treatment with high doses of domperidone and methylprednisolone. *Lancet* 1984; **ii:** 1336–7.
3. Weaving A, *et al.* Seizures after antiemetic treatment with high dose domperidone: report of four cases. *BMJ* 1984; **288:** 1728.
4. Roussak JB, *et al.* Cardiac arrest after treatment with intravenous domperidone. *BMJ* 1984; **289:** 1579.
5. Osborne RJ, *et al.* Cardiotoxicity of intravenous domperidone. *Lancet* 1985; **ii:** 385.
6. Rocha CMG, Barbosa MM. QT interval prolongation associated with the oral use of domperidone in an infant. *Pediatr Cardiol* 2005; **26:** 720–3.

Effects on the endocrine system. There have been reports of galactorrhoea with gynaecomastia[1] or mastalgia[2,3] generally associated with raised serum-prolactin concentrations. Gynaecomastia without galactorrhoea has also been reported.[4]

1. Van der Steen M, *et al.* Gynaecomastia in a male infant given domperidone. *Lancet* 1982; **ii:** 884–5.
2. Cann PA, *et al.* Galactorrhoea as side effect of domperidone. *BMJ* 1983; **286:** 1395–6.
3. Cann PA, *et al.* Oral domperidone: double blind comparison with placebo in irritable bowel syndrome. *Gut* 1983; **24:** 1135–40.
4. Keating JP, Rees M. Gynaecomastia after long-term administration of domperidone. *Postgrad Med J* 1991; **67:** 401–2.

Extrapyramidal effects. There are reports of extrapyramidal symptoms,[1,2] including acute dystonic reactions[3] and neuroleptic malignant syndrome[4] in individual patients given domperidone.

1. Sol P, *et al.* Extrapyramidal reactions due to domperidone. *Lancet* 1980; **ii:** 802.