Desloratadine *(BAN, USAN, rINN)*

Descarboethoxyloratadine; Desloratadin; Desloratadina; Desloratadinum; Sch-34117. 8-Chloro-6,11-dihydro-11-(4-piperidylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

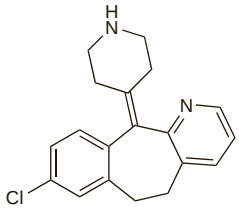
Дезлоратадин

$C_{19}H_{19}ClN_2$ = 310.8.

CAS — 100643-71-8.

ATC — R06AX27.

ATC Vet — QR06AX27.



Profile

Desloratadine, the major, active metabolite of loratadine (p.583), is a non-sedating antihistamine. Desloratadine is used in the symptomatic relief of allergic conditions including rhinitis (p.565) and urticaria (p.565).

Desloratadine is given in an oral dose of 5 mg once daily.

It is also used with a decongestant such as pseudoephedrine sulfate.

For dosage in children, and in hepatic or renal impairment, see below.

◊ References.

1. McClellan K, Jarvis B. Desloratadine. *Drugs* 2001; **61:** 789–96.
2. Simons FER, ed. Desloratadine: clinical pharmacokinetics of a novel H receptor antagonist. *Clin Pharmacokinet* 2002; **41** (suppl 1): 1–44.
3. Limon L, Kockler DR. Desloratadine: a nonsedating antihistamine. *Ann Pharmacother* 2003; **37:** 237–46. Correction. *ibid.*; 454.
4. Murdoch D, *et al.* Desloratadine: an update of its efficacy in the management of allergic disorders. *Drugs* 2003; **63:** 2051–77.
5. Berger WE. The safety and efficacy of desloratadine for the management of allergic disease. *Drug Safety* 2005; **28:** 1101–18.
6. Canonica GW, *et al.* Efficacy of desloratadine in the treatment of allergic rhinitis: a meta-analysis of randomized, double-blind, controlled trials. *Allergy* 2007; **62:** 359–66.

Administration in children. In the UK, desloratadine is licensed for use in children aged 1 year and over in the treatment of allergic rhinitis and urticaria; in the USA, it may be given to those aged 6 months and over for perennial allergic rhinitis and urticaria and to those aged 2 years and over for seasonal allergic rhinitis.

Regardless of indication, oral doses of desloratadine are as follows:

- children aged 6 to 11 months: 1 mg once daily
- those aged 1 to 5 years: 1.25 mg once daily
- those aged 6 to 11 years: 2.5 mg once daily.

Administration in hepatic or renal impairment. US licensed product information recommends that patients with hepatic or renal impairment should be given desloratadine 5 mg orally on alternate days initially.

Breast feeding. Desloratadine is distributed into breast milk and consequently UK and US licensed product information does not recommend its use during breast feeding. For a discussion of the use of *loratadine* in breast feeding, see under Adverse Effects and Precautions, p.583.

Pregnancy. Desloratadine was not teratogenic in *animal* studies; however, product information recommends it should be used with caution, if at all, in pregnant women.

For a discussion of the use of loratadine in pregnancy, see under Adverse Effects and Precautions, p.583.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Aerius; Azomyr†; Frenaler; Hexaler; Novo Alerpriv; ***Austral.:*** Claramax; ***Austria:*** Aerius; ***Belg.:*** Aerius; ***Braz.:*** Desalex; ***Canad.:*** Aerius; ***Chile:*** Aerius; Mailen; Neo Larmax; Neoclaritine; Neohysticlar; Rinaid; Rinofilax; ***Cz.:*** Aerius; Azomyr; Neoclarityn; ***Denm.:*** Aerius; ***Fin.:*** Aerius; ***Fr.:*** Aerius; ***Ger.:*** Aerius; ***Gr.:*** Aerius; Neoclarityn†; ***Hong Kong:*** Aerius; ***Hung.:*** Aerius; ***India:*** D-Loratin; Des-OD; Deslor; ***Indon.:*** Aerius; ***Irl.:*** Neoclarityn; ***Israel:*** Aerius; ***Ital.:*** Aerius; Azomyr; ***Malaysia:*** Aerius; ***Mex.:*** Aviant; Azomyr; ***Neth.:*** Aerius; Azomyr; Neoclarityn; ***Norw.:*** Aerius; ***NZ:*** Aerius; Claramax; ***Philipp.:*** Aerius; ***Pol.:*** Aerius; ***Port.:*** Aerius; Azomyr; Neoclarityn; ***Rus.:*** Aerius (Эриус); ***S.Afr.:*** Deselex; ***Singapore:*** Aerius; Desalex†; ***Spain:*** Aerius; Azomyr; ***Swed.:*** Aerius; ***Switz.:*** Aerius; ***Thai.:*** Aerius; ***Turk.:*** Aerius; ***UK:*** Neoclarityn; ***USA:*** Clarinex; ***Venez.:*** Aerius; Desalex; Deslorat; Esparflin; Mailen.

Multi-ingredient: ***Cz.:*** Aerinaze; ***USA:*** Clarinex-D.

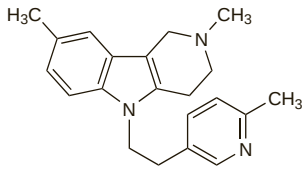
Dimebolin

Dimebol; Dimeboline; Dimebon; Dimebone. 2,3,4,5-Tetrahydro-2,8-dimethyl-5-[2-(6-methyl-3-pyridinyl)ethyl]-1*H*-pyrido[4,3-*b*]indole.

Димеболин

$C_{21}H_{25}N_3$ = 319.4.

CAS — 3613-73-8 (dimebolin); 14292-23-0 (dimebolin x-hydrochloride).



Profile

Dimebolin is an antihistamine that is reported to also have neuroprotective effects. It is under investigation as the dihydrochloride in the treatment of Alzheimer's disease and Huntington's disease.

◊ References.

1. Doody RS, *et al.* Effect of dimebon on cognition, activities of daily living, behaviour, and global function in patients with mild-to-moderate Alzheimer's disease: a randomised, double-blind, placebo-controlled study. *Lancet* 2008; **372:** 207–15.

Dimenhydrinate *(BAN, rINN)*

Chloranautine; Dimenhidrinát; Dimenhidrinat; Dimenhidrinatas; Dimenhidrinato; Dimenhydramina; Dimenhydrinaatti; Dimenhydrinát; Dimenhydrinat; Diménhydrinate; Dimenhydrinatum; Diphenhydramine Teoclate; Diphenhydramine Theoclate. The diphenhydramine salt of 8-chlorotheophylline .

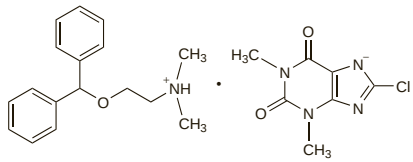
Дименгидринат

$C_{17}H_{21}NO,C_7H_7ClN_4O_2$ = 470.0.

CAS — 523-87-5.

ATC — R06AA02.

ATC Vet — QR06AA02.



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

Ph. Eur. 6.2 (Dimenhydrinate). A white or almost white, crystalline powder or colourless crystals. M.p. 102° to 106°. Slightly soluble in water; freely soluble in alcohol. A saturated solution in water has a pH of 7.1 to 7.6.

USP 31 (Dimenhydrinate). A white, odourless, crystalline powder. Slightly soluble in water; freely soluble in alcohol and in chloroform; sparingly soluble in ether.

Incompatibility. Dimenhydrinate has been reported to be incompatible in solution with a wide range of compounds; those most likely to be encountered include: aminophylline, glycopyrronium bromide, hydrocortisone sodium succinate, hydroxyzine hydrochloride, meglumine adipiodone, some phenothiazines, and some soluble barbiturates.

Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561.

Effects on the eyes. Dimenhydrinate 100 mg, given at 4-hourly intervals for 3 doses, was found to affect colour discrimination, night vision, reaction time, and stereopsis.[1]

1. Luria SM, *et al.* Effects of aspirin and dimenhydrinate (Dramamine) on visual processes. *Br J Clin Pharmacol* 1979; **7:** 585–93.

Porphyria. Dimenhydrinate has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Pregnancy. For discussion of the use of antihistamines in pregnancy, including a suggestion of a relationship between cardiovascular defects or inguinal hernia and dimenhydrinate exposure, see p.563.

Interactions

As for the sedating antihistamines in general, p.563.

Uses and Administration

Dimenhydrinate, a monoethanolamine derivative, is a sedating antihistamine with antimuscarinic and significant sedative effects. It is used mainly as an antiemetic in the prevention and treatment of motion sickness (p.564). It is also used for the symptomatic treatment of nausea and vertigo caused by Ménière's disease and other vestibular disturbances (see Vertigo, p.565).

The usual oral dose of dimenhydrinate is 50 to 100 mg, given 3 or 4 times daily. For the prevention of motion sickness, the first dose should be given at least 30 minutes before travelling. Typical doses for children, according to age, are: 2 to up to 6 years, 12.5 to 25 mg every 6 to 8 hours to a maximum of 75 mg daily (in some countries lower doses of 6.25 to 12.5 mg are given two or three times daily); 6 to 12 years, 25 to 50 mg every 6 to 8 hours to a maximum of 150 mg daily (again lower doses are used in some countries).

Dimenhydrinate may be given parenterally in usual doses of 50 mg, a concentration of 5% being used for intramuscular injection and 0.5% for slow intravenous injection (usually over 2 minutes). Children have been given dimenhydrinate by intramuscular or slow intravenous injection in a dose of 1.25 mg/kg four times daily to a maximum of 300 mg daily.

Dimenhydrinate has also been given by the rectal route.

Preparations

BP 2008: Dimenhydrinate Tablets;
USP 31: Dimenhydrinate Injection; Dimenhydrinate Syrup; Dimenhydrinate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Dr Amin; Dramamine; Marine†; ***Austral.:*** Dramamine; ***Austria:*** Emedyl; Nausex; Travel-Gum; Vertirosan; ***Belg.:*** Paranausine; Vagomine†; ***Braz.:*** Dimedri†; Dramamine; Dramavit†; Dramin; Emebrid†; Neodrin; ***Canad.:*** Anti-Nauseant; Childrens Motion Sickness Liquid; Dinate; Gravol; Nauseatol; Novo-Dimenate; Travamine†; Travel Aid†; ***Chile:*** Mareamin; ***Cz.:*** Travel-Gum; ***Denm.:*** Anautin; ***Fr.:*** Dramamine; Nausicalm; ***Ger.:*** Dimen†; Reisegold†; Reisetabletten; Rodavan S; RubieMen†; Superpep; Vertigo-Vomex; Vomacur; Vomex A; ***Gr.:*** Dravom†; Drimen; Travelgum; Vomex A; ***Hong Kong:*** Dimate; Dimenate; Garcol; Gravol; Novomin; ***Hung.:*** Daedalon; Daedalonetta; ***India:*** Dramnate; Gravol; ***Indon.:*** Dramamine; Stopmun; ***Irl.:*** Dramamine†; ***Israel:*** Dramamine†; Travamin; ***Ital.:*** Lomarin; Motozina; Travelgum; Valontan; Xamamina; ***Malaysia:*** Dimenate; Dramamine; Driminate; Hydrinate; Novomin†; Setmenate†; ***Mex.:*** Apo-Mina; Dimetin-F†; Dimicaps; Dramamine; Unitril†; Vomisin; ***NZ:*** Dramamine; ***Philipp.:*** Gravol; ***Pol.:*** Aviomarin; ***Port.:*** Dramamine†; Draminal; Enjomin; Viabom; Vomidrine; ***Rus.:*** Dramina (Драмина); ***Singapore:*** Dimenate; Dramamine†; ***Spain:*** Biodramina; Cinfamar; Contramareo; Travel Well; ***Swed.:*** Amosyt; ***Switz.:*** Antemin; Dramamine†; Trawell; ***Thai.:*** Denim; Dimeno; Dimin†; Dramamine; Gravol; Motivan; Nausamine; Navamin; Phrachedi; Vominar†; ***Turk.:*** Anti-Em; Dramamine; Xamamine; ***UAE:*** Dizinil; ***UK:*** Arlevert; ***USA:*** Calm-X; Dimetabs; Dinate; Dramamine; Dramanate; Dymenate; Hydrate†; Triptone; ***Venez.:*** Dramamine†; Viajesan.

Multi-ingredient: ***Austral.:*** Travacalm; ***Austria:*** Neo-Emedyl; Synkapton; Vertirosan Vitamin B ; ***Braz.:*** Dramavit B6†; Dramin B-6; Dramin B-6 DL; Nausicalm; Nausilon B6; ***Canad.:*** Gravergol†; ***Cz.:*** Arlevert; Migraeflux; ***Fr.:*** Mercalm; ***Ger.:*** Arlevert; Migraeflux N; Migraeflux orange N; ***Gr.:*** Vertigo-Vomex; ***Hong Kong:*** Gravergol†; Rhinocap; ***Hung.:*** Arlevert; ***Indon.:*** Dramasine; ***Mex.:*** Bomine; ***Spain:*** Acetuber; Biodramina Cafeina; Cinfamar Cafeina; Saldeva; Salvarina; Sin Mareo x 4; ***Switz.:*** Agorhino†; Antemin compositum; Dramamine-compositum†; Gem Voyage Dragees contre les maux de voyage; Rhinocap; Trawell compositum; ***Thai.:*** Roxine.

Dimetindene Maleate *(BANM, rINNM)*

Dimethindene Maleate *(USAN)*; Dimethpyrindene Maleate; Dimethylpyrindene Maleate; Dimetindeenimaleaatti; Dimetinden Maleat; Dimétindène, maléate de; Dimetindeni maleas; Dimetindenmaleat; Dimetindén-maleát; Dimetinden-maleinát; Dimetindeno maleatas; Maleato de dimetindeno; NSC-107677; Su-6518. *NN*-Dimethyl-2-{3-[1-(2-pyridyl)ethyl]-1*H*-inden-2-yl}ethylamine hydrogen maleate.

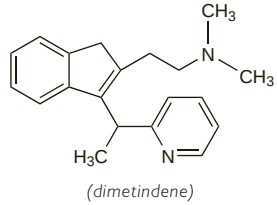
Диметиндена Малеат

$C_{20}H_{24}N_2,C_4H_4O_4$ = 408.5.

CAS — 5636-83-9 (dimetindene); 3614-69-5 (dimetindene maleate).

ATC — D04AA13; R06AB03.

ATC Vet — QD04AA13; QR06AB03.



(dimetindene)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Dimetindene Maleate). A white to almost white, crystalline powder. Slightly soluble in water; soluble in methyl alcohol. Protect from light.

Profile
Dimetindene maleate, an alkylamine derivative, is a sedating antihistamine (p.561); it is mildly sedative and is reported to have mast-cell stabilising properties. It is used for the symptomatic relief of allergic conditions including urticaria and angioedema (p.565) and rhinitis (p.565), and in pruritic skin disorders (p.565). It is also used in compound preparations for the symptomatic treatment of coughs and the common cold (p.564).

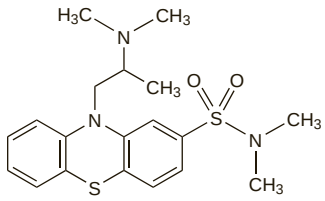
Dimetindene maleate is given in an oral dose of 1 to 2 mg three times daily; modified-release preparations are also available. It may also be given by the intravenous route. Dimetindene maleate is applied topically as a 0.1% gel or lotion although, as with other antihistamines, there is a risk of sensitisation. It is used in a strength of 0.025% in compound nasal preparations.

Preparations
Proprietary Preparations (details are given in Part 3)
Austria: Fenistil; ***Belg.:*** Fenistil; ***Cz.:*** Fenistil; ***Ger.:*** Fenistil; ***Gr.:*** Fenistil; ***Hung.:*** Fenistil; ***India:*** Foristal; ***Indon.:*** Fenistil; ***Israel:*** Fenistil; ***Ital.:*** Fenistil; ***Neth.:*** Fenistil; ***Norw.:*** Fenistil†; ***Philipp.:*** Fenistil; ***Pol.:*** Fenistil; ***Port.:*** Fenistil; Neostil; ***Rus.:*** Fenistil (Фенистил); ***Spain:*** Fenistil; ***Switz.:*** Fenistil; ***Thai.:*** Fenistil; ***Turk.:*** Fenistil; ***Venez.:*** Fenistil†.

Multi-ingredient: ***Arg.:*** Vibragel; ***Austria:*** Trimedil; Vibrocil; ***Belg.:*** Vibrocil; ***Braz.:*** Gripen; Trimedal; ***Cz.:*** Vibrocil; ***Ger.:*** Vibrocil†; ***Gr.:*** Vibrocil-S; ***Hong Kong:*** Vibrocil†; ***Hung.:*** Otrivin Allergia; Vibrocil; ***Israel:*** Vibrocil; ***Ital.:*** Vibrocil; ***Pol.:*** Otrivin Allergy; ***Port.:*** Vibrocil; ***Rus.:*** Vibrocil (Виброцил); ***S.Afr.:*** Vibrocil; Vibrocil-S; ***Switz.:*** Vibrocil.

Dimetotiazine Mesilate *(BANM, rINNM)*
Dimethothiazine Mesylate; Dimétotiazine, Mésilate de; Dimetotiazini Mesilas; Fonazine Mesylate *(USAN)*; IL-6302 (dimetotiazine); Mesilato de dimetotiazina; 8599-RP (dimetotiazine). 10-(2-Dimethylaminopropyl)-*NN*-dimethylphenothiazine-2-sulphonamide methanesulphonate.

Диметотиазина Мезилат
$C_{19}H_{25}N_3O_2S_2,CH_3SO_3H$ = 487.7.
CAS — 7456-24-8 (dimetotiazine); 7455-39-2 (dimetotiazine mesilate).
ATC — N02CX05.
ATC Vet — QN02CX05.



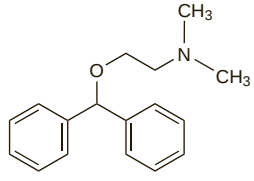
(dimetotiazine)

Profile
Dimetotiazine mesilate, a phenothiazine derivative, is a sedating antihistamine (p.561). It has been used for the symptomatic relief of hypersensitivity reactions, in pruritic skin disorders, and in the management of headaches including migraine.

Preparations
Proprietary Preparations (details are given in Part 3)
Indon.: Migristene; ***Mex.:*** Migristene.

Diphenhydramine *(BAN, rINN)*
Benzhydramine; Difenhidramina; Difenhydramiini; Difenhydramin; Diphénhydramine; Diphenhydraminum. 2-Benzhydryloxy-*NN*-dimethylethylamine.

Дифенгидрамин
$C_{17}H_{21}NO$ = 255.4.
CAS — 58-73-1.
ATC — D04AA32; R06AA02.
ATC Vet — QD04AA32; QR06AA02.



Pharmacopoeias. In *Jpn.*

Diphenhydramine Citrate *(BANM, rINNM)*
Benzhydramine Citrate; Citrato de difenhidramina; Diphénhydramine, Citrate de; Diphenhydramini Citras.

Дифенгидрамина Цитрат
$C_{17}H_{21}NO,C_6H_8O_7$ = 447.5.
CAS — 88637-37-0.
ATC — D04AA32; R06AA02.
ATC Vet — QD04AA32; QR06AA02.

Pharmacopoeias. In *US.*
USP 31 (Diphenhydramine Citrate). Store in airtight containers. Protect from light.

Diphenhydramine Di(acefyllinate) *(rINNM)*
Benzhydramine Di(acefyllinate); Bietanautine; Di(acefilinato) de difenhidramina; Diphénhydramine Diacéfylline; Diphenhydramine Di(acephyllinate); Diphenhydramini Diacefyllinas. Diphenhydramine bis(theophyllin-7-ylacetate).

Дифенгидрамина Диацефиллинат
$C_{17}H_{21}NO,2C_9H_{10}N_4O_4$ = 731.8.
CAS — 6888-11-5.
ATC — D04AA32; R06AA02.
ATC Vet — QD04AA32; QR06AA02.

NOTE. The name Etanautine has been applied both to diphenhydramine monoacefyllinate and to ethylbenzhydramine, an antimuscarinic formerly used in the symptomatic treatment of parkinsonism.

Diphenhydramine Hydrochloride *(BANM, rINNM)*
Benzhydramine Hydrochloride; Difenhidramin Hidroklorür; Difenhidramin-hidroklorid; Difenhidramino hidrochloridas; Difenhydramiinihydrokloridi; Difenhydramin-hydrochlorid; Difenhydraminhydroklorid; Difenhydraminy chlorowodorek; Dimedrolum; Diphénhydramine, chlorhydrate de; Diphenhydramini hydrochloridum; Diphenhydraminium Chloride; Hidrocloruro de difenhidramina.

Дифенгидрамина Гидрохлорид
$C_{17}H_{21}NO,HCl$ = 291.8.
CAS — 147-24-0.
ATC — D04AA32; R06AA02.
ATC Vet — QD04AA32; QR06AA02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn,* and *US.*
Jpn also includes Diphenhydramine Tannate.
Ph. Eur. 6.2 (Diphenhydramine Hydrochloride). A white or almost white, crystalline powder. Very soluble in water; freely soluble in alcohol. A 5% solution in water has a pH of 4.0 to 6.0. Protect from light.
USP 31 (Diphenhydramine Hydrochloride). A white, odourless, crystalline powder. It slowly darkens on exposure to light. Soluble 1 in 1 of water, 1 in 2 of alcohol and of chloroform, and 1 in 50 of acetone; very slightly soluble in ether and in benzene. Its solutions are neutral to litmus. Store in airtight containers. Protect from light.

Incompatibility. Diphenhydramine hydrochloride has been reported to be incompatible with amphotericin B, cefmetazole sodium, cefalotin sodium, hydrocortisone sodium succinate, some soluble barbiturates, some contrast media, and solutions of alkalis or strong acids.

Adverse Effects and Precautions
As for the sedating antihistamines in general, p.561.

Abuse. Reports of the abuse of diphenhydramine hydrochloride.

1. Anonymous. Is there any evidence that Benylin syrup is addictive? *BMJ* 1979; **1:** 459.
2. Smith SG, Davis WM. Nonmedical use of butorphanol and diphenhydramine. *JAMA* 1984; **252:** 1010.
3. Feldman MD, Behar M. A case of massive diphenhydramine abuse and withdrawal from use of the drug. *JAMA* 1986; **255:** 3119–20.
4. de Nesnera AP. Diphenhydramine dependence: a need for awareness. *J Clin Psychiatry* 1996; **57:** 136–7.
5. Dinndorf PA, *et al.* Risk of abuse of diphenhydramine in children and adolescents with chronic illnesses. *J Pediatr* 1998; **133:** 293–5.

Extrapyramidal disorders. Reports of dystonic extrapyramidal reactions to diphenhydramine.

1. Lavenstein BL, Cantor FK. Acute dystonia: an unusual reaction to diphenhydramine. *JAMA* 1976; **236:** 291.
2. Santora J, Rozek S. Diphenhydramine-induced dystonia. *Clin Pharm* 1989; **8:** 471.
3. Roila F, *et al.* Diphenhydramine and acute dystonia. *Ann Intern Med* 1989; **111:** 92–3.

Overdosage. In an evaluation of 136 cases, one fatal, of intoxication with diphenhydramine, the plasma concentration was correlated with frequency or extent of symptoms.[1] The most common symptom was impaired consciousness; psychosis, seizures, antimuscarinic symptoms such as mydriasis, tachycardia, and tachyarrhythmias, and respiratory failure were also observed. The positive association between dose and frequency and severity of symptoms was confirmed in a more recent study;[2] it was also found that severe symptoms were more likely to occur when 1 g or more of diphenhydramine had been taken.

There have been reports[3,4] of rhabdomyolysis as an effect of oral diphenhydramine overdosage. The liberal application of a lotion containing diphenhydramine produced acute delirium with visual and auditory hallucinations in a 9-year-old boy[5] and similar effects were seen in 3 children with varicella-zoster infection following the topical application of diphenhydramine (2 of these children also received oral diphenhydramine).[6]

1. Köppel C, Tenczer J. Clinical symptomatology of diphenhydramine overdose: an evaluation of 136 cases in 1982 to 1985. *Clin Toxicol* 1987; **25:** 53–70.
2. Radovanovic D, *et al.* Dose-dependent toxicity of diphenhydramine overdose. *Hum Exp Toxicol* 2000; **19:** 489–95.
3. Hampel G, *et al.* Myoglobinuric renal failure due to drug-induced rhabdomyolysis. *Hum Toxicol* 1983; **2:** 197–203.
4. Haas CE, *et al.* Rhabdomyolysis and acute renal failure following an ethanol and diphenhydramine overdose. *Ann Pharmacother* 2003; **37:** 538–42.
5. Filloux F. Toxic encephalopathy caused by topically applied diphenhydramine. *J Pediatr* 1986; **108:** 1018–20.
6. Chan CYJ, Wallander KA. Diphenhydramine toxicity in three children with varicella-zoster infection. *DICP Ann Pharmacother* 1991; **25:** 130–2.

Porphyria. Diphenhydramine has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Pregnancy. A pregnant woman who was receiving diphenhydramine hydrochloride 150 mg daily for a pruritic rash gave birth to an infant who developed diarrhoea and generalised tremulousness 5 days later.[1] The delay in appearance of withdrawal symptoms was considered to be due to reduced activity of glucuronyl conjugating enzymes in the first few days of life.
For discussion of the use of antihistamines in pregnancy, including a suggestion of a relationship between inguinal hernia or genito-urinary malformations and diphenhydramine exposure, see p.563. See also under Interactions, below, for a report of perinatal death possibly associated with temazepam and diphenhydramine.

1. Parkin DE. Probable Benadryl withdrawal manifestations in a new-born infant. *J Pediatr* 1974; **85:** 580.

Interactions
As for the sedating antihistamines in general, p.563. Diphenhydramine inhibits the cytochrome P450 isoenzyme CYP2D6 that is partly responsible for the metabolism of some beta blockers including metoprolol and the antidepressant venlafaxine.

Benzodiazepines. There has been a report[1] suggesting that a reduction in *temazepam* metabolism caused by diphenhydramine may have contributed to perinatal death after ingestion of these drugs by the mother.

1. Kargas GA, *et al.* Perinatal mortality due to interaction of diphenhydramine and temazepam. *N Engl J Med* 1985; **313:** 1417–18.

Pharmacokinetics
Diphenhydramine hydrochloride is well absorbed from the gastrointestinal tract, although high first-pass metabolism appears to affect systemic availability. Peak plasma concentrations are achieved about 1 to 4 hours after oral doses. Diphenhydramine is widely distributed throughout the body including the CNS. It crosses the placenta and has been detected in breast milk. Diphenhydramine is highly bound to plasma proteins. Metabolism is extensive. Diphenhydramine is excreted mainly in the urine as metabolites; little is excreted as unchanged drug. The elimination half-life has been reported to range from 2.4 to 9.3 hours.

◊ References.

1. Glazko AJ, *et al.* Metabolic disposition of diphenhydramine. *Clin Pharmacol Ther* 1974; **16:** 1066–76.
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4. Scavone JM, *et al.* Pharmacokinetics and pharmacodynamics of diphenhydramine 25 mg in young and elderly volunteers. *J Clin Pharmacol* 1998; **38:** 603–9.

Uses and Administration
Diphenhydramine, a monoethanolamine derivative, is a sedating antihistamine with antimuscarinic and pronounced sedative properties. It is used for the symptomatic relief of allergic conditions including urticaria and angioedema (p.565), rhinitis (p.565) and conjunctivitis (p.564), and in pruritic skin disorders (p.565). It is also used for its antiemetic properties in the treatment of nausea and vomiting (p.564), particularly in the prevention and treatment of motion sickness (when