

effective, especially in the elderly, in whom the inappropriate prescribing of drugs for postural instability needs to be avoided. Such measures include improving visual acuity, balance exercises, and the use of walking aids.

The most widely used drugs for acute vertigo are the antihistamines. They may have a direct action on the inner ear besides acting centrally. Antimuscarinic actions may contribute to their activity; antimuscarinics, especially hyoscine, have a long history of use in vertigo. Antihistamines used in the treatment of vertigo include buclizine, cyclizine, dimenhydrinate, diphenhydramine, meclozine, and promethazine. Cinnarizine and flunarizine are also used for vertigo although they are devoid of any significant antimuscarinic actions; their activity may be due to calcium-channel blockade. Phenothiazines such as prochlorperazine are also used to control any associated vomiting. Benzodiazepines including diazepam have been given in acute severe attacks. However their prolonged use in those with chronic symptoms is of questionable value.

Vasodilators may be of benefit in the treatment of vertigo of vascular aetiology. Parenteral or sublingual histamine was formerly widely used, and betahistine is still advocated especially for vertigo associated with Ménière's disease. Nicotinic alcohol has also been used.

#### References.

1. Rascol O, *et al.* Antivertigo medications and drug-induced vertigo: a pharmacological review. *Drugs* 1995; **50**: 777–91.
2. Luxon LM. Vertigo: new approaches to diagnosis and management. *Br J Hosp Med* 1996; **56**: 519–20 and 537–41.
3. Luxon LM. Assessment and management of vertigo. *Prescribers' J* 1998; **38**: 87–97.
4. Baloh RW. Vertigo. *Lancet* 1998; **352**: 1841–6.
5. Hain TC, Uddin M. Pharmacological treatment of vertigo. *CNS Drugs* 2003; **17**: 85–100.

## Acrivastine (BAN, USAN, rINN)

Acrivastin; Acrivastina; Acrivastinum; Akrivastini; Akrivastin; BVV-825C. (E)-3-[6-[(E)-3-Pyrrolidin-1-yl-1-p-tolylprop-1-enyl]-2-pyridyl]acrylic acid.

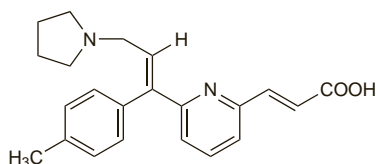
Акривастин

$C_{22}H_{24}N_2O_2 = 348.4$ .

CAS — 87848-99-5.

ATC — R06AX18.

ATC Vet — QR06AX18.



## Adverse Effects and Precautions

As for the non-sedating antihistamines in general, p.561. Acrivastine should be given with care in renal impairment; UK licensed product information recommends that it should not be given to patients with significant renal impairment, while product information in other countries, such as Switzerland for example, contra-indicates its use in those with a creatinine clearance of less than 50 mL/minute. Acrivastine should not be used in patients hypersensitive to triprolidine.

**Sedation.** For a discussion of the sedative effects of antihistamines see p.562.

## Interactions

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

## Pharmacokinetics

Acrivastine is well absorbed from the gastrointestinal tract; peak plasma concentrations are achieved in about 1.5 hours. The plasma half-life of acrivastine is about 1.5 hours and the drug does not appear to cross the blood-brain barrier to a significant extent. Acrivastine along with an active metabolite is excreted principally in the urine.

## Uses and Administration

Acrivastine is a non-sedating antihistamine structurally related to triprolidine. It does not have any significant sedative or antimuscarinic actions. It is used for the symptomatic relief of allergic conditions such as rhinitis (p.565) and various types of urticaria (p.565) when it is given in oral doses of 8 mg three times daily. It is also used with a decongestant such as pseudoephedrine hydrochloride.

**Administration in renal impairment.** See Precautions, above

## Preparations

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

**Austria:** Semprex; **Cz:** Semprex; **Denm:** Benadryl; **Fin:** Benadryl; **Semprex**; **Hong Kong:** Semprex; **Italy:** Semprex; **Malaysia:** Semprex; **Neth:** Semprex; **Philipp:** Semprex; **Rus:** Semprex (Семпрекс); **S.Afr:** Semprex; **Singapore:** Semprex; **Swed:** Semprex; **Switz:** Semprex; **Thai:** Semprex; **Turk:** Semprex; **UK:** Benadryl Allergy Relief.

**Multi-ingredient:** **Austria:** Duact; **Denm:** Duact; **Fin:** Duact; **Turk:** Duact; **UK:** Benadryl Plus; **USA:** Semprex-D.

## Alimemazine Tartrate (BANM, rNNM)

Alimémazine, Tartrate d'; Alimemazini Tartras; Tartrato de alimemazina; Trimeprazine Tartrate. NN-Dimethyl-2-methyl-3-(phenothiazin-10-yl)propylamine tartrate.

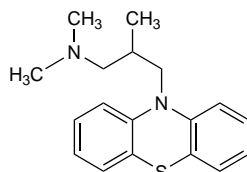
Алимемазина Тартрат

$(C_{18}H_{22}N_2S)_2 \cdot C_4H_6O_6 = 747.0$ .

CAS — 84-96-8 (alimemazine); 4330-99-8 (alimemazine tartrate).

ATC — R06AD01.

ATC Vet — QR06AD01.



(alimemazine)

**Pharmacopoeias.** In *Br.*, *Fr.*, *Jpn.*, and *US*.

**BP 2008** (Alimemazine Tartrate). A white or slightly cream powder. It darkens on exposure to light. Freely soluble in water; sparingly soluble in alcohol; very slightly soluble in ether. A 2% solution in water has a pH of 5.0 to 6.5. Protect from light.

**USP 31** (Trimeprazine Tartrate). A white to off-white, odourless, crystalline powder. Soluble 1 in 2 of water, 1 in 20 of alcohol, 1 in 5 of chloroform, and 1 in 1800 of ether; very slightly soluble in benzene. Store in airtight containers. Protect from light.

## Adverse Effects and Precautions

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

**Children.** There have been reports of adverse effects in children given alimemazine tartrate orally. Fatal malignant hyperthermia<sup>1</sup> and severe cardiovascular depression<sup>2</sup> have occurred after its use for premedication, and severe respiratory and CNS depression<sup>3</sup> after use as a postoperative sedative. Doses in these 3 reports ranged from 2.4 to 4.4 mg/kg. Although unconfirmed, a possible association between phenothiazine sedatives and sudden infant death syndrome has also been suggested (see Promethazine Hydrochloride, p.588). Alimemazine tartrate is no longer licensed in the UK for short-term sedation in children and it is recommended that it should not be used in infants less than 2 years of age (but see below). The maximum recommended oral dose for premedication of children aged 2 to 7 years is 2 mg/kg. There has been a warning<sup>4</sup> that the use of alimemazine for deep sedation in diagnostic and therapeutic procedures in children is associated with prolonged drowsiness and that standards of monitoring, starvation, and postprocedural care should be similar to those with general anaesthesia.

1. Moyes DG. Malignant hyperpyrexia caused by trimeprazine. *Br J Anaesth* 1973; **45**: 1163–4.
2. Loan WB, Cuthbert D. Adverse cardiovascular response to oral trimeprazine in children. *BMJ* 1985; **290**: 1548–9.
3. Mann NP. Trimeprazine and respiratory depression. *Arch Dis Child* 1981; **56**: 481–2.
4. Cray SH, Hinton W. Sedation for investigations: prolonged effect of chloral and trimeprazine. *Arch Dis Child* 1994; **71**: 179.

**Pregnancy.** For a discussion of the use of antihistamines in pregnancy, including studies involving phenothiazines, see p.563.

## Interactions

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

## Uses and Administration

Alimemazine, a phenothiazine derivative, is a sedating antihistamine with antiemetic activity and pronounced sedative effects. It also has some antimuscarinic actions. It is used mainly for the relief of urticaria (p.565) and pruritus (p.565), and, in the UK, for pre-operative medication in children. Alimemazine may also be used in compound preparations for the symptomatic treatment of coughs (p.564).

Alimemazine tartrate is given orally; doses in the UK are given as the amount of alimemazine tartrate, while those in some other countries are expressed in terms of the equivalent amount of alimemazine. Alimemazine tartrate 25 mg is equivalent to about 20 mg of alimemazine.

- The adult dose of alimemazine tartrate used for the relief of **urticaria** and **pruritus** in the UK is 10 mg two or three times daily; up to 100 mg daily has been given in refractory cases. Elderly patients are given 10 mg once or twice daily and children over 2 years of age 2.5 to 5 mg three or four times daily. Despite the view that alimemazine should not be given to younger children (see above), and although not licensed in the UK, the *BNFC* suggests that 250 micrograms/kg (maximum of 2.5 mg) three or four times daily may be given to those aged 6 months to 2 years for the relief of urticaria and pruritus, but only under specialist care.

- Doses used in the USA have been lower, even allowing for them being expressed in terms of alimemazine. The adult dose was the equivalent of alimemazine 2.5 mg four times daily. Children in the USA 3 years of age and over have been given 2.5 mg at night or three times daily. However, it appears that proprietary preparations are no longer available in the USA.

- The usual recommended dose in the UK for **pre-medication** in children aged 2 to 7 years is up to 2 mg/kg given about one to two hours before the operation.

**Anaesthesia.** Alimemazine tartrate may be used for anaesthetic premedication (see p.563) in children if the oral route is preferred to the more usual parenteral route of other phenothiazine antihistamines. Adverse effects have, however, been reported in children (see under Adverse Effects and Precautions, above), and in the UK alimemazine tartrate is not licensed for use in infants less than 2 years of age.

**Insomnia.** Antihistamines such as alimemazine tartrate have been used as alternatives to benzodiazepines for the short-term treatment of insomnia (p.564), particularly for children. However, their antimuscarinic side-effects may prove troublesome.

Regimens involving a short course of alimemazine tartrate in high dosage were tried in order to alter the sleep pattern of children with sleeping difficulties.<sup>1,2</sup> Adverse effects have, however, been reported in children (see under Adverse Effects and Precautions, above). The UK product is no longer indicated for short-term sedation in children and should not be used in infants less than 2 years of age.

1. Valman HB. ABC of 1 to 7 (revised): sleep problems. *BMJ* 1987; **294**: 828–30.
2. Anonymous. What can be done for night waking in children? *Lancet* 1987; **ii**: 948–9.

## Preparations

**BP 2008:** Alimemazine Tablets; Paediatric Alimemazine Oral Solution; Strong Paediatric Alimemazine Oral Solution;

**USP 31:** Trimeprazine Tartrate Syrup; Trimeprazine Tartrate Tablets.

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

**Austral:** Chemists Own Peetaxil; **Vallergan;** **Belg:** Theralene; **Canad:** Panectyl; **Fr:** Theralene; **Ger:** Repeltin; **Ir:** Vallergan; **Neth:** Nedeltran; **Norw:** Vallergan; **NZ:** Vallergan; **S.Afr:** Vallergan; **Spain:** Variangil; **Swed:** Theralen; **UK:** Vallergan.

**Multi-ingredient:** **Fr:** Sirop Teyssedre; Theralene Pectoral Nourisson;.

**Antazoline** (BAN, rINN)

Antazolini; Antazolin; Antazolina; Antazolinum. *N*-Benzyl-*N*-(2-imidazolin-2-ylmethyl)aniline.

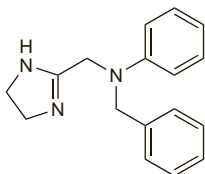
Антазолин

$C_{17}H_{19}N_3 = 265.4$ .

CAS — 91-75-8.

ATC — R01AC04; R06AX05.

ATC Vet — QR01AC04; QR06AX05.

**Antazoline Hydrochloride** (BANM, rINNM)

Antazolinihydrokloridi; Antazolin hydrochlorid; Antazoline, chlorhydrate d'; Antazolin-hidroklorid; Antazolinhydroklorid; Antazolini Hydrochloricum; Antazolini hydrochloridum; Antazolinium Chloride; Antazolino hidrokloridas; Antazolin chlorowodorek; Hidrokloruro de antazolina; Imidamine Hydrochloride; Phenazolinum.

Антазолина Гидрохлорид

$C_{17}H_{19}N_3 \cdot HCl = 301.8$ .

CAS — 2508-72-7.

ATC — R01AC04; R06AX05.

ATC Vet — QR01AC04; QR06AX05.

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

**Ph. Eur. 6.2** (Antazoline Hydrochloride). A white or almost white crystalline powder. Sparingly soluble in water; soluble in alcohol; slightly soluble in dichloromethane.

**Antazoline Mesilate** (BANM, rINNM)

Antazoline, Mésilate d'; Antazoline Mesylate; Antazoline Methanesulphonate; Antazolini Mesilas; Antazolin mezylan; Imidamine Mesylate; Mesilato de antazolina.

Антазолина Мезилаат

$C_{17}H_{19}N_3 \cdot CH_3SO_3H = 361.5$ .

CAS — 3131-32-6.

ATC — R01AC04; R06AX05.

ATC Vet — QR01AC04; QR06AX05.

**Pharmacopoeias.** In *Pol.*

**Antazoline Phosphate** (BANM, rINNM)

Antazolin Fosfat; Antazoline, Phosphate d'; Antazolini Phosphas; Fosfato de antazolina; Imidamine Phosphate.

Антазолина Фосфат

$C_{17}H_{19}N_3 \cdot H_3PO_4 = 363.3$ .

CAS — 154-68-7.

ATC — R01AC04; R06AX05.

ATC Vet — QR01AC04; QR06AX05.

**Pharmacopoeias.** In *US.*

**USP 31** (Antazoline Phosphate). A white to off-white crystalline powder. Soluble in water; practically insoluble in ether and in benzene; sparingly soluble in methyl alcohol. pH of a 2% solution in water is between 4.0 and 5.0. Store in airtight containers.

**Antazoline Sulfate** (rINNM)

Antazoline, Sulfate d'; Antazoline Sulphate (BANM); Antazolini Sulfas; Imidamine Sulphate; Sulfato de antazolina.

Антазолина Сульфат

$(C_{17}H_{19}N_3)_2 \cdot H_2SO_4 \cdot 2H_2O = 664.8$ .

CAS — 24359-81-7 (anhydrous antazoline sulfate).

ATC — R01AC04; R06AX05.

ATC Vet — QR01AC04; QR06AX05.

NOTE. The above molecular formula is that provided in the *It. P.* Other sources give a molecular formula of  $C_{17}H_{19}N_3 \cdot H_2SO_4$ .

**Pharmacopoeias.** In *It.*

**Adverse Effects and Precautions**

As for the antihistamines in general, p.561.

**Hypersensitivity.** Reports of acute interstitial pneumonitis (with fever, rash, and dyspnoea)<sup>4</sup> and of immune thrombocytopenic purpura<sup>2</sup> were attributed to hypersensitivity reactions after the oral use of antazoline.

1. Pahissa A, *et al.* Antazoline-induced allergic pneumonitis. *BMJ* 1979; **2**: 1328.

2. Nielsen JL, *et al.* Immune thrombocytopenia due to antazoline (Antistina). *Allergy* 1981; **36**: 517-19.

**Uses and Administration**

Antazoline, an ethylenediamine derivative, is an antihistamine used topically for the treatment of allergic conjunctivitis (p.564).

The symbol † denotes a preparation no longer actively marketed

It is used as the hydrochloride, phosphate, or sulfate in eye drops, most commonly in a concentration of 0.5%; the mesilate has also been used. Antazoline salts are often used with a vasoconstrictor such as naphazoline hydrochloride or nitrate or xylometazoline hydrochloride.

The hydrochloride and sulfate salts of antazoline have been used topically for the treatment of minor skin irritations, but as with other antihistamines there is a risk of sensitisation. The hydrochloride has also been given by mouth.

**Preparations**

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

**Multi-ingredient:** **Austral:** Albalon-A; Antistine-Privine; In A Wink Allergy†; **Austria:** Histophtal; **Belg:** Zincfin Anthistaminicum†; **Canad:** Albalon-A; Vasocon-A†; **Chile:** Albasol A†; Bacitopic Compuesto; Nasomim; Oftalino; Red Off Plus; Rinobanedi; **Spersallerg:** **Cz:** Sanonin-Analergin; **Spersallerg:** **Denm:** Ansal; Antistina-Privin; Sesal; **Fin:** Antistin-Privin†; **Ger:** Allergopos N; Antistin-Privin; **Spersallerg:** **Gr:** **Spersallerg:** **Hong Kong:** **Spersallerg:** **Hung:** **Spersallerg:** **Indon:** Indofrin-A; **Ir:** Otrivine-Antist; **RBC:** **Israel:** Antistin-Privin†; **Ital:** Antistin-Privina; **Malaysia:** Alergoftal; **Napha A:** **Spersallerg:** **Mex:** Midazol Ofteno; Oftalino†; **Zincfin-A:** **Norw:** **Spersallerg:** **NZ:** Albalon-A†; **Otrivine-Antist;** **Philipp:** **Spersallerg:** **Pol:** Dermophenazoli; Oftophenazoli; Rhinophenazoli; **Spersallerg:** **Port:** Alergitalmina; **Rus:** Sanonin-Analergin (Санонин-аналергин); **Spersallerg** (Сперсальверг); **S.Afr:** Albalon-A†; Antistin-Privin; Covosan; Gemini; Oculer; Safyr Bleu Antihistamine†; **Spersallerg:** **Zincfin-A:** **Singapore:** Antistin-Privin; **Spersallerg:** **Spain:** Alergoftal; **Swed:** Antasten-Privin; **Switz:** Antistin-Privin; **Spersallerg:** **Thai:** Antazallerg; **Histaoph:** Opa-Hist†; **Opisil-A:** **Spersallerg:** **Turk:** Alergoftal; **Sulfarhin:** **UK:** Otrivine-Antist; **USA:** Antazoline-V; Vasocon-A.

**Astemizole** (BAN, USAN, rINN)

Astemitsoli; Astemizol; Astemizolas; Astémizole; Astemizolum; Asztemizol; MJD-30. 1-(4-Fluorobenzyl)-2-[[1-(4-methoxyphenyl)-4-piperidyl]amino]benzimidazole.

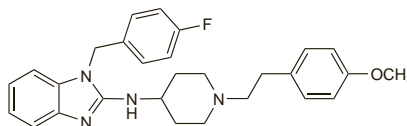
АСТЕМИЗОЛ

$C_{28}H_{31}FN_4O = 458.6$ .

CAS — 68844-77-9.

ATC — R06AX11.

ATC Vet — QR06AX11.



NOTE. The code R-43512 has been used to describe both astemizole and its metabolite tecaastemizole (norastemizole).

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

**Ph. Eur. 6.2** (Astemizole). A white or almost white powder. Practically insoluble in water; soluble in alcohol; freely soluble in dichloromethane and in methyl alcohol. Protect from light.

**USP 31** (Astemizole). Store in airtight containers.

**Adverse Effects and Precautions**

As for the non-sedating antihistamines in general, p.561. Increased appetite and weight gain have been reported with astemizole.

Ventricular arrhythmias, including torsade de pointes, have occurred rarely with astemizole, particularly in association with raised blood concentrations (see Arrhythmias below) and as a result the drug has been withdrawn from the market in most countries. To reduce the risk of developing such arrhythmias recommendations were that licensed doses should not be exceeded, and that it should be avoided in patients with cardiac or significant hepatic disease, with hypokalaemia or other electrolyte imbalance, or with known or suspected prolonged QT interval. Use with drugs liable to interfere with the hepatic metabolism of astemizole, other potentially arrhythmogenic drugs including those that prolong the QT interval, and drugs likely to cause electrolyte imbalance, is **contra-indicated** (see Interactions below).

**Arrhythmias.** Although severe life-threatening cardiovascular effects including torsade de pointes and other ventricular arrhythmias were initially reported mainly after substantial overdoses of astemizole, such reactions have also occurred rarely with doses as low as 20 to 30 mg daily and even as low as 10 mg daily in those with possible predisposing factors. There has been a report<sup>1</sup> of astemizole-induced torsade de pointes in a 15-year-old girl who claimed to have taken 10 mg daily for 10 weeks but pharmacokinetic data were more consistent with acute ingestion of higher doses. There have also been several reports of cardiotoxicity after accidental overdosage with astemizole in children.<sup>2-4</sup>

Although the drug is now withdrawn in the UK, recommendations were made by the UK CSM to reduce the risk of developing serious arrhythmias<sup>5-7</sup> (see Adverse Effects above for details). It was considered that astemizole should be stopped immediately in patients who experience syncope, and appropriate clinical

evaluation including ECG monitoring instituted, because syncope has preceded or accompanied severe arrhythmias in some cases. Convulsions in patients taking astemizole may also be related to cardiovascular effects.<sup>8</sup>

Studies have suggested that astemizole induces ventricular arrhythmias by inhibiting cardiac potassium channels which results in prolongation of the QT interval, a risk factor for developing arrhythmias.<sup>9</sup> For further discussion, see p.562.

1. Simons FER, *et al.* Astemizole-induced torsade de pointes. *Lancet* 1988; **ii**: 624.
2. Hoppu K, *et al.* Accidental astemizole overdose in young children. *Lancet* 1991; **338**: 538-40.
3. Tobin JR, *et al.* Astemizole-induced cardiac conduction disturbances in a child. *JAMA* 1991; **266**: 2737-40.
4. Wiley JF, *et al.* Cardiotoxic effects of astemizole overdose in children. *J Pediatr* 1992; **120**: 799-802.
5. CSM. Ventricular arrhythmias due to terfenadine and astemizole. *Current Problems* 35 1992. Also available at: [http://www.mhra.gov.uk/home/idcplg?IdcService=GET\\_FILE&dDocName=CON2024453&RevisionSelectionMethod=LatestReleased](http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024453&RevisionSelectionMethod=LatestReleased) (accessed 14/07/08)
6. CSM/MCA. Drug-induced prolongation of the QT interval. *Current Problems* 1996; **22**: 2. Also available at: [http://www.mhra.gov.uk/home/idcplg?IdcService=GET\\_FILE&dDocName=CON2024453&RevisionSelectionMethod=LatestReleased](http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024453&RevisionSelectionMethod=LatestReleased) (accessed 14/07/08)
7. CSM/MCA. Astemizole (Hismanal): only available on prescription. *Current Problems* 1999; **25**: 2. Also available at: [http://www.mhra.gov.uk/home/idcplg?IdcService=GET\\_FILE&dDocName=CON2023233&RevisionSelectionMethod=LatestReleased](http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023233&RevisionSelectionMethod=LatestReleased) (accessed 19/05/06)
8. Clark A, Love H. Astemizole-induced ventricular arrhythmias: an unexpected cause of convulsions. *Int J Cardiol* 1991; **33**: 165-7.
9. Rankin AC. Non-sedating antihistamines and cardiac arrhythmia. *Lancet* 1997; **350**: 1115-16.

**Overdosage.** Severe cardiac events have been associated with astemizole overdosage (see Arrhythmias, above); management is mainly supportive. The absorption of astemizole from the gastrointestinal tract can be prevented by giving activated charcoal<sup>1</sup> but because astemizole is rapidly absorbed it would need to be given as soon as possible after poisoning. Haemodialysis does not appear to increase the clearance of astemizole.

1. Laine K, *et al.* The effect of activated charcoal on the absorption and elimination of astemizole. *Hum Exp Toxicol* 1994; **13**: 502-5.

**Porphyria.** Astemizole is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

**Sedation.** For discussion of the sedative effects of antihistamines see p.562.

**Interactions**

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

Astemizole should not be given with drugs that inhibit its hepatic metabolism because of the increased risk of serious ventricular arrhythmias. These drugs include the imidazole and triazole antifungals such as ketoconazole and itraconazole, and the macrolide antibacterials clarithromycin, erythromycin, troleanomycin, and possibly other macrolides. Others, similarly to terfenadine (p.591), may include serotonin reuptake inhibitors, HIV-protease inhibitors, NNRTIs, and zileuton. The metabolism of astemizole may also be inhibited by grapefruit juice and use together should be avoided.

Use with other potentially arrhythmogenic drugs (including those that prolong the QT interval) such as antiarrhythmics, tricyclic antidepressants, the antimalarials halofantrine and quinine, antipsychotics, cisapride, and the beta blocker sotalol should be avoided, as should diuretics that cause electrolyte imbalances such as hypokalaemia. The use of terfenadine and astemizole together is not recommended.

**Pharmacokinetics**

Absorption of astemizole from the gastrointestinal tract is rapid and is reduced by food. First-pass metabolism is extensive, therefore plasma concentrations of unchanged drug are very low. The plasma concentration of astemizole plus metabolites takes about 4 to 8 weeks to reach steady state. The metabolism of astemizole is mediated through the cytochrome P450 enzyme system by the isoenzymes CYP3A4, CYP2D6, and CYP2A6. The elimination half-life of astemizole and its metabolites at steady state is about 19 days. Unchanged astemizole is highly bound to plasma proteins and does not appear to cross the blood-brain barrier to a significant extent. Desmethylastemizole, the major metabolite of astemizole, has histamine H<sub>1</sub>-receptor-blocking activity; tecaastemizole (norastemizole) is another active metabolite. The metabolites of astemizole are excreted slowly in the urine and faeces, and undergo enterohepatic recycling. Virtually none of an oral dose is excreted as unchanged drug.

**Uses and Administration**

Astemizole, a piperidine derivative, is a non-sedating antihistamine with a very long duration of action. It does not have significant sedative or antimuscarinic actions. Astemizole has been used for the symptomatic relief of allergic conditions including rhinitis (p.565) and conjunctivitis (p.564), and skin disorders such as urticaria (p.565). Preparations of astemizole have now