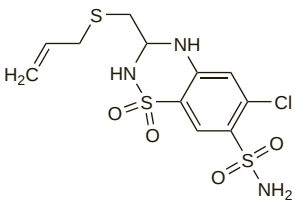
Altizide *(rINN)* ⊗

Althiazide *(USAN)*; Altizida; Altizidum; P-1779. 3-Allylthiomethyl-6-chloro-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

Альтизид

$C_{11}H_{14}ClN_3O_4S_3$ = 383.9.

CAS — 5588-16-9.



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

Ph. Eur. 6.2 (Altizide). A white or almost white powder. Practically insoluble in water; soluble in methyl alcohol; practically insoluble in dichloromethane. It exhibits polymorphism.

Profile

Altizide is a thiazide diuretic (see Hydrochlorothiazide, p.1307) that is used in the treatment of oedema and hypertension. It is frequently used with spironolactone.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Belg.:*** Aldactazine; ***Fr.:*** Aldactazine; Practazin; Spiroctazine; ***Port.:*** Aldactazine; ***Spain:*** Aldactacine.

Ambrisentan *(BAN, rINN)*

Ambrisentán; Ambrisentanum; BSF-208075; LU-208075. (+)-(2*S*)-2-[(4,6-Dimethylpyrimidin-2-yl)oxy]-3-methoxy-3,3-diphenylpropanoic acid.

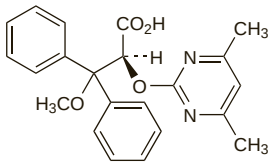
Амбризентан

$C_{22}H_{22}N_2O_4$ = 378.4.

CAS — 177036-94-1.

ATC — C02KX02.

ATC Vet — QC02KX02.



Adverse Effects and Precautions

As for Bosentan, p.1235.

Interactions

Ambrisentan is a substrate for a number of enzymes and transporters and interactions could potentially occur with inducers or inhibitors of the cytochrome P450 isoenzymes CYP3A4 and CYP2C19, P-glycoprotein, uridine diphosphate glucuronosyltransferases, and organic anion transporting polypeptide (OATP).

Pharmacokinetics

Ambrisentan is rapidly absorbed from the gastrointestinal tract and peak plasma concentrations occur about 2 hours after oral doses. It is about 99% bound to plasma proteins. Ambrisentan is excreted mainly by the liver, although the relative contribution of hepatic metabolism and biliary excretion is not known. The terminal elimination half-life is about 15 hours.

Uses and Administration

Ambrisentan is an endothelin receptor antagonist (p.1155) with similar actions to bosentan (p.1235), although it has a higher selectivity for the endothelin ET_A-receptor. It is used in the management of pulmonary hypertension functional class II or III (p.1179). It is given orally in an initial dose of 5 mg once daily; the dose may be increased to 10 mg once daily if tolerated.

◊ References.

1. Galié N, *et al.* Ambrisentan therapy for pulmonary arterial hypertension. *J Am Coll Cardiol* 2005; **46:** 529–35.
2. Vatter H, Seifert V. Ambrisentan, a non-peptide endothelin receptor antagonist. *Cardiovasc Drug Rev* 2006; **24:** 63–76.
3. Barst RJ. A review of pulmonary arterial hypertension: role of ambrisentan. *Vasc Health Risk Manag* 2007; **3:** 11–22.
4. Anonymous. Ambrisentan (Letairis) for pulmonary arterial hypertension. *Med Lett Drugs Ther* 2007; **49:** 87–8.

Preparations

Proprietary Preparations (details are given in Part 3)

UK: Volibris; ***USA:*** Letairis.

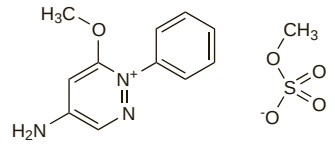
Amezinium Metilsulfate *(rINN)* ⊗

Ametsiniummetilsulfaatti; Amezinii Metilsulfas; Amezinium Methylsulphate; Amézinium, Métilsulfate d'; Ameziniummetilsulfat; Metilsulfato de amezinio. 4-Amino-6-methoxy-1-phenylpyridazinium methylsulfate.

Амезиния Метилсульфат

$C_{12}H_{15}N_3O_5S$ = 313.3.

CAS — 30578-37-1.



Profile

Amezinium metilsulfate is a sympathomimetic (p.1407) used for its vasopressor effects in the treatment of hypotensive states (p.1174). It is given orally in a usual dose of 10 mg up to three times daily. It has also been given by slow intravenous injection.

Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Regulton; ***Ger.:*** Regulton; Supratonin.

Amiloride Hydrochloride

(BANM, USAN, rINNM) ⊗

Amilorid Hidroklorür; Amilorid hydrochlorid dihydrát; Amiloride, chlorhydrate d'; Amilorid-hidroklorid; Amiloridhydroklorid; Amiloridi hydrochloridum; Amiloridi Hydrochloridum Dihydricum; Amiloridihydrokloridi; Amilorido hidrochloridas; Amilorydu chlorowodorek; Amipramizide; Cloridrato de Amilorida; Hidrocloruro de amilorida; MK-870. *N*-Amidino-3,5-diamino-6-chloropyrazine-2-carboxamide hydrochloride dihydrate.

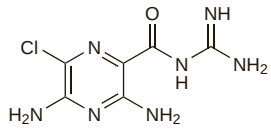
Амилорида Гидрохлорид

$C_6H_8ClN_7O,HCl,2H_2O$ = 302.1.

CAS — 2609-46-3 (amiloride); 2016-88-8 (anhydrous amiloride hydrochloride); 17440-83-4 (amiloride hydrochloride dihydrate).

ATC — C03DB01.

ATC Vet — QC03DB01.



(amiloride)

NOTE. Compounded preparations of amiloride hydrochloride may be represented by the following names:

- Co-amilofruse (*BAN*)—amiloride hydrochloride 1 part and furosemide 8 parts (w/w)
- Co-amilozide (*BAN*)—amiloride hydrochloride 1 part and hydrochlorothiazide 10 parts (w/w)
- Co-amilozide (*PEN*)—amiloride hydrochloride and hydrochlorothiazide.

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

Ph. Eur. 6.2 (Amiloride Hydrochloride). A pale yellow to greenish-yellow powder. Slightly soluble in water and in dehydrated alcohol. Protect from light.

USP 31 (Amiloride Hydrochloride). A yellow to greenish-yellow, odourless or practically odourless, powder. Slightly soluble in water; insoluble in acetone, in chloroform, in ether, and in ethyl acetate; freely soluble in dimethyl sulfoxide; sparingly soluble in methyl alcohol.

Adverse Effects

Amiloride can cause hyperkalaemia, particularly in elderly patients, diabetics, and patients with renal impairment. Hyponatraemia has been reported in patients taking amiloride with other diuretics. Amiloride may cause nausea, vomiting, abdominal pain, diarrhoea or constipation, paraesthesia, thirst, dizziness, skin rash, pruritus, weakness, muscle cramps, headache, and minor psychiatric or visual changes. Orthostatic hypotension and rises in blood-urea-nitrogen concentrations have been reported. Other adverse effects of amiloride may include alopecia, cough, dyspnoea, jaundice, encephalopathy, impotence, angina pectoris, arrhythmias, and palpitations.

Effects on electrolyte balance. There have been reports of metabolic acidosis associated with amiloride or triamterene[1] and with co-amilozide.[2]

1. Kushner RF, Sitrin MD. Metabolic acidosis: development in two patients receiving a potassium-sparing diuretic and total parenteral nutrition. *Arch Intern Med* 1986; **146:** 343–5.
2. Wan HH, Lye MDW. Moduretic-induced metabolic acidosis and hyperkalaemia. *Postgrad Med J* 1980; **56:** 348–50.

POTASSIUM. Hyperkalaemia is the main adverse effect when amiloride is given alone but may also occur when amiloride is given with a potassium-wasting diuretic. Severe hyperkalaemia has been reported during co-amilozide therapy, particularly in patients with renal impairment[1,2] and has been accompanied by metabolic acidosis in one such patient.[3]

1. Whiting GFM, *et al.* Severe hyperkalaemia with Moduretic. *Med J Aust* 1979; **1:** 409.
2. Jaffey L, Martin A. Malignant hyperkalaemia after amiloride/hydrochlorothiazide treatment. *Lancet* 1981; **i:** 1272.
3. Wan HH, Lye MDW. Moduretic-induced metabolic acidosis and hyperkalaemia. *Postgrad Med J* 1980; **56:** 348–50.

SODIUM. For reports of severe hyponatraemia in patients taking diuretics such as amiloride with potassium-wasting diuretics, see Hydrochlorothiazide, p.1308.

Effects on the skin. For a report of photosensitivity reactions in patients taking co-amilozide, see Hydrochlorothiazide, p.1309.

Precautions

Amiloride has the same precautions as spironolactone with regard to hyperkalaemia (see p.1400). It should be stopped at least 3 days before glucose-tolerance tests are performed in patients who may have diabetes mellitus because of the risks of provoking severe hyperkalaemia.

Interactions

There is an increased risk of hyperkalaemia if amiloride is given with potassium supplements or with other potassium-sparing diuretics. Hyperkalaemia may also occur in patients given amiloride with ACE inhibitors, angiotensin II receptor antagonists, NSAIDs, ciclosporin, or trilostane. In patients taking amiloride with NSAIDs or ciclosporin the risk of nephrotoxicity may also be increased. Diuretics may reduce the excretion of lithium and increase the risk of lithium toxicity, but this does not appear to occur with amiloride. Severe hyponatraemia may occur in patients taking a potassium-sparing diuretic with a thiazide; this risk may be increased in patients taking chlorpropamide. Amiloride may reduce the ulcer-healing properties of carbenoxolone. As with other diuretics, amiloride may enhance the effects of other antihypertensive drugs.

Digoxin. For the effects of amiloride on digoxin clearance, see p.1262.

Quinidine. For a report of amiloride producing arrhythmias in patients receiving quinidine, see p.1384.

Pharmacokinetics

Amiloride is incompletely absorbed from the gastrointestinal tract; bioavailability is about 50% and is reduced by food. It is not significantly bound to plasma proteins and has a plasma half-life of 6 to 9 hours; the terminal half-life may be 20 hours or more. It is excreted unchanged by the kidneys.

◊ General references.

1. Weiss P, *et al.* The metabolism of amiloride hydrochloride in man. *Clin Pharmacol Ther* 1969; **10:** 401–6.

Hepatic impairment. In patients with acute hepatitis the terminal half-life of amiloride was 33 hours compared with 21 hours in healthy subjects.[1] The proportion of the dose excreted in the urine was increased from 49 to 80%.

1. Spahn H, *et al.* Pharmacokinetics of amiloride in renal and hepatic disease. *Eur J Clin Pharmacol* 1987; **33:** 493–8.

Renal impairment. Studies of the pharmacokinetics of amiloride[1,2] have reported an increase in terminal elimination half-life from 20 hours in healthy subjects to 100 hours in patients with end-stage renal disease. The natriuretic effect of amiloride was reduced[1] in patients with creatinine clearance below 50 mL/minute. In patients with renal impairment amiloride could aggravate potassium retention due to renal disease. Studies in elderly patients have found increased half-life[3] and steady-state concentrations[4] associated with reduced renal function.

1. Knauf H, *et al.* Limitation on the use of amiloride in early renal failure. *Eur J Clin Pharmacol* 1985; **28:** 61–6.

2. Spahn H, *et al.* Pharmacokinetics of amiloride in renal and hepatic disease. *Eur J Clin Pharmacol* 1987; **33:** 493–8.
3. Sabanathan K, *et al.* A comparative study of the pharmacokinetics and pharmacodynamics of atenolol, hydrochlorothiazide and amiloride in normal young and elderly subjects and elderly hypertensive patients. *Eur J Clin Pharmacol* 1987; **32:** 53–60.
4. Ismail Z, *et al.* The pharmacokinetics of amiloride-hydrochlorothiazide combination in the young and elderly. *Eur J Clin Pharmacol* 1989; **37:** 167–71.

Uses and Administration

Amiloride is a weak diuretic that appears to act mainly on the distal renal tubules. It is described as potassium-sparing since, like spironolactone, it increases the excretion of sodium and reduces the excretion of potassium. Unlike spironolactone, however, it does not act by specifically antagonising aldosterone. Amiloride does not inhibit carbonic anhydrase. It takes effect about 2 hours after oral dosage and its diuretic action reaches a peak in 6 to 10 hours and has been reported to persist for about 24 hours.

Amiloride diminishes the kaliuretic effects of other diuretics, and may produce an additional natriuretic effect. It is mainly used as an adjunct to thiazide diuretics such as hydrochlorothiazide and loop diuretics such as furosemide, to conserve potassium in those at risk from hypokalaemia during the long-term treatment of oedema associated with hepatic cirrhosis (including ascites, p.1159) and heart failure (p.1165). It is also used with other diuretics in the treatment of hypertension (p.1171). Diuretic-induced hypokalaemia and its management, including the role of potassium-sparing diuretics such as amiloride, is discussed under Effects on Electrolyte Balance in the Adverse Effects of Hydrochlorothiazide, p.1308. Amiloride is sometimes used to manage hypokalaemia in primary hyperaldosteronism (p.1402).

Amiloride by inhalation has also been investigated in the management of cystic fibrosis patients with lung disease (see below).

In the treatment of **oedema** amiloride is given orally as the hydrochloride and doses are expressed in terms of the anhydrous substance. 1 mg of anhydrous hydrochloride is equivalent to about 1.14 mg of the hydrated substance. Treatment may be started with a dose of 5 to 10 mg daily, increased, if necessary, to a maximum of 20 mg daily. An initial dose of 2.5 mg once daily may be used in patients already taking other diuretics or antihypertensives. Similar doses to those given for oedema are used to reduce potassium loss in patients receiving thiazide or loop diuretics.

Potassium supplements should not be given.

Cystic fibrosis. Pulmonary disease is the major cause of mortality in cystic fibrosis (p.166). Experimental treatment aimed at modifying the pulmonary disease process has included giving amiloride by inhalation.[1,2] No evidence of pulmonary or systemic toxicity was seen in 14 patients treated for 25 weeks.[1] The mechanism of action is unclear but could be the sodium-channel blocking effect[1] or anti-inflammatory effects[3] of amiloride. Concern has been expressed[4] over possible consequences of the inhibition of endogenous urokinase by amiloride although others[5] considered this to be unlikely at the concentrations studied. However, a systematic review[6] found no evidence that amiloride was of clinical benefit.

1. Knowles MR, *et al.* A pilot study of aerosolized amiloride for the treatment of lung disease in cystic fibrosis. *N Engl J Med* 1990; **322:** 1189–94.
2. App EM, *et al.* Acute and long-term amiloride inhalation in cystic fibrosis lung disease: a rational approach to cystic fibrosis therapy. *Am Rev Respir Dis* 1990; **141:** 605–12.
3. Gallo RL. Aerosolized amiloride for the treatment of lung disease in cystic fibrosis. *N Engl J Med* 1990; **323:** 996–7.
4. Henkin J. Aerosolized amiloride for the treatment of lung disease in cystic fibrosis. *N Engl J Med* 1990; **323:** 997.
5. Knowles MR, *et al.* Aerosolized amiloride for the treatment of lung disease in cystic fibrosis. *N Engl J Med* 1990; **323:** 997–8.
6. Burrows E, *et al.* Sodium channel blockers for cystic fibrosis. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 28/04/08).

Diabetes insipidus. Thiazide diuretics are commonly used in nephrogenic diabetes insipidus (p.2179) and NSAIDs may also be employed; both result in an overall decrease in urine production. Hydrochlorothiazide with amiloride has been reported to be at least as effective as hydrochlorothiazide plus indometacin in 5 patients.[1] In addition, amiloride obviated the need for potassium supplements. Hydrochlorothiazide with amiloride was also effective and well tolerated in a group of 4 children with nephrogenic diabetes insipidus who were treated for up to 5 years.[2]

1. Knoers N, Monnens LAH. Amiloride-hydrochlorothiazide versus indomethacin-hydrochlorothiazide in the treatment of nephrogenic diabetes insipidus. *J Pediatr* 1990; **117:** 499–502.
2. Kirchlechner V, *et al.* Treatment of nephrogenic diabetes insipidus with hydrochlorothiazide and amiloride. *Arch Dis Child* 1999; **80:** 548–52.

Renal calculi. Patients with idiopathic hypercalciuria and a history of renal calculi (p.2181) are usually given a thiazide diuretic such as hydrochlorothiazide to reduce calcium excretion. In patients with calcium oxalate calculi an inherited cellular defect in oxalate transport may also be involved and this might be corrected by amiloride.[1]

1. Baggio B, *et al.* An inheritable anomaly of red-cell oxalate transport in "primary" calcium nephrolithiasis correctable with diuretics. *N Engl J Med* 1986; **314:** 599–604.

Preparations

BP 2008: Amiloride Tablets; Co-amilofruse Tablets; Co-amilozide Oral Solution; Co-amilozide Tablets;
USP 31: Amiloride Hydrochloride and Hydrochlorothiazide Tablets; Amiloride Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Kaluril; Midamor; ***Austria:*** Midamor; ***Canad.:*** Midamor; ***Cz.:*** Amiclaran; ***Denm.:*** Amikal†; Nirulid; ***Fin.:*** Medamor†; ***Fr.:*** Modamide; ***NZ:*** Midamor; ***Swed.:*** Midamor†; ***Switz.:*** Midamor†; ***UK:*** Amilamont; ***USA:*** Midamor.

Multi-ingredient: ***Arg.:*** Amiloclor†; Diflux; Diur Pot; Diurex A; Errolon A; Furdiuren†; Hidrenox A; Lasiride; Moducren†; Moduretic; Nuriban A; Plenacor D; Prenomod†; Ren-Ur; Vericordin Compuesto; ***Austral.:*** Amizide; Moduretic; ***Austria:*** Aldoretic; Amiloral/HCT; Amiloretik; Amilorid comp; Amilostad HCT; Lanuretic; Loradur; Moducrin; Moduretic; ***Belg.:*** Belidral†; Co-Amiloride; Frusamil; Kalten†; Moduretic; ***Braz.:*** Amiretic; Diupress; Diurezin-A; Diurisa; Moduretic; ***Canad.:*** Apo-Amilzide; Gen-Amilazide; Moduret; Novamilor; Nu-Amilzide; ***Chile:*** Furdiuren; Hidrium; Hidropid; ***Cz.:*** Amicloton; Amilorid/HCT; Apo-Amilzide; Limorid†; Loradur; Moduretic; Rhefluin; ***Denm.:*** Amilco; Buram; Frusamil; Moduretic†; Sparkal; ***Fin.:*** Amitrid; Diuramin; Diurex; Miloride; Moduretic; Sparkal; ***Fr.:*** Logirene; Moducren; Moduretic; ***Ger.:*** Amilocomp beta; Amiloretik; Amilorid comp; Amilorid/HCT; Amilozid†; Aquaretic†; Diaphal; Diursan; durarese†; Esmalorid†; Moducrin; Moduretik; Tensoflux; ***Gr.:*** Frumil; Ividol; Moduretic; Tiaden; ***Hong Kong:*** Amilco†; Amithiazide; Apo-Amilzide; Moducren; Moduretic; Navispare; Sefaretic; ***Hung.:*** Amilorid Comp; Amilozid-B; ***India:*** Biduret; Frumil; Hipres-D; ***Indon.:*** Lorinid; ***Irl.:*** Amilco†; Buram; Fru-Co; Frumil; Lasoride†; Moducren; Moduret; ***Israel:*** Kaluril; ***Ital.:*** Moduretic; ***Malaysia:*** Ami-Hydrotride; Amizide; Apo-Amilzide; Moduretic; ***Mex.:*** Moduretic; ***Neth.:*** Moduretic; ***Norw.:*** Moduretic; Normorix; ***NZ:*** Amizide; Frumil; ***Pol.:*** Tialorid; ***Port.:*** Aldoretic†; Amiloride Composto†; Chibretico†; Diurene; Moducren†; Moduretic; ***S.Afr.:*** Adco-Retic; Amiloretic; Betaretic; Hexaretic; Moducren; Moduretic; Servatrin; ***Singapore:*** Apo-Amilzide; ***Spain:*** Ameride; Diuzine; Kalten; ***Swed.:*** Amiloferm; Moduretic; Normorix; Sparkal; ***Switz.:*** Agorex†; Amilo-basan†; Amiloride/HCTZ; Betadiur†; Co-Amilorid†; Comilorid; Ecodurex; Escoretic; Frumil†; Grodurex; Kalten; Moducren; Moduretic; Rhefluin; ***Thai.:*** Bilduretic; Hydrozide Plus; Hyperretic; Miduret†; Milorex†; Miretic; Modulan†; Moduretic; Moure-M; Poli-Uretic; Renase; Sefaretic; ***Turk.:*** Moduretic; ***UK:*** Amil-Co; Aridil; Burinex A; Froop Co†; Fru-Co; Frumil; Kalten; Komil; Lasoride†; Moducren†; Moduret; Moduretic; Navispare; ***USA:*** Moduretic; ***Venez.:*** Furdiuren; Moduretic.

Amiodarone *(BAN, USAN, rINN)*

Amiodaron; Amiodarona; Amiodaroni; Amiodaronum; L-3428; 51087-N; SKF-33134-A. 2-Butylbenzofuran-3-yl 4-(2-diethylaminoethoxy)-3,5-di-iodophenyl ketone.

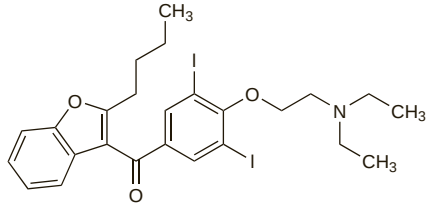
Амиодарон

$C_{25}H_{29}I_2NO_3$ = 645.3.

CAS — 1951-25-3.

ATC — C01BD01.

ATC Vet — QC01BD01.



Amiodarone Hydrochloride *(BANM, rINNM)*

Amiodaron Hidroklorür; Amiodarone, chlorhydrate d'; Amiodaron-hidroklorid; Amiodaron-hydrochlorid; Amiodaronhydroklorid; Amiodaroni hydrochloridum; Amiodaronihydrokloridi; Amjodarono hidrochloridas; Hidrocloruro de amiodarona.

Амиодарона Гидрохлорид

$C_{25}H_{29}I_2NO_3$,HCl = 681.8.

CAS — 19774-82-4.

ATC — C01BD01.

ATC Vet — QC01BD01.

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

Ph. Eur. 6.2 (Amiodarone Hydrochloride). A white or almost white, fine crystalline powder. Very slightly soluble in water; sparingly soluble in alcohol; freely soluble in dichloromethane; soluble in methyl alcohol. Store at a temperature not exceeding 30°. Protect from light.

Adsorption. Amiodarone is known to be adsorbed by PVC, although the amount of adsorption has varied in different studies. A study[1] using amiodarone hydrochloride 600 micrograms/mL in glucose 5% found that the concentration fell by 10% in 3 hours followed by a steady decrease to 60% of the initial concentration after 5 days when stored in flexible PVC bags at ambient temperature.[1] However, another study[2] using amiodarone hydrochloride 1.8 to 2 mg/mL in glucose 5% found only that the concentration remained 97.3% of the initial value after 24 hours in PVC infusion bags. In the first study, perfusion of the solution through PVC giving sets resulted in the concentration falling to 82% after 15 minutes, whereas the second study found the concentration fell to 95.1% after 1 hour but then returned to the initial value. No loss was noted in either study when glass or rigid PVC containers were used, suggesting that the losses were caused by the plasticiser, di-2-ethylhexylphthalate (DEHP). Amiodarone may also leach out DEHP and other plasticisers, and it has been suggested that bags and tubing containing DEHP should not be used for giving amiodarone in order to minimise patient exposure.

1. Weir SJ, *et al.* Sorption of amiodarone to polyvinyl chloride infusion bags and administration sets. *Am J Hosp Pharm* 1985; **42:** 2679–83.
2. Peters PG, Hayball PJ. A comparative analysis of the loss of amiodarone from small and large volume PVC and non-PVC infusion systems. *Anaesth Intensive Care* 1990; **18:** 241–5.

Incompatibility. Amiodarone injection has been reported to be incompatible with aminophylline,[1] flucloxacillin,[2] heparin,[3] and sodium bicarbonate.[4] A further study[5] reported incompatibility with ampicillin/sulbactam sodium, ceftazidime sodium, digoxin, furosemide, imipenem/cilastatin sodium, magnesium sulfate, piperacillin sodium, piperacillin/tazobactam sodium, potassium phosphate, and sodium phosphate. UK licensed product information states that it is incompatible with sodium chloride solutions.

1. Hasegawa GR, Eder JF. Visual compatibility of amiodarone hydrochloride injection with other injectable drugs. *Am J Hosp Pharm* 1984; **41:** 1379–80.
2. Taylor A, Lewis R. Amiodarone and injectable drug incompatibility. *Pharm J* 1992; **248:** 533.
3. Cairns CJ. Incompatibility of amiodarone. *Pharm J* 1986; **236:** 68.
4. Korth-Bradley JM. Incompatibility of amiodarone hydrochloride and sodium bicarbonate injections. *Am J Health-Syst Pharm* 1995; **52:** 2340.
5. Chalmers JR, *et al.* Visual compatibility of amiodarone hydrochloride injection with various intravenous drugs. *Am J Health-Syst Pharm* 2001; **58:** 504–6.

Stability. An oral suspension prepared from tablets[1] and containing amiodarone hydrochloride 5 mg/mL was stable for 3 months at 4° and 6 weeks at 25°.

1. Nahata MC. Stability of amiodarone in an oral suspension stored under refrigeration and at room temperature. *Ann Pharmacother* 1997; **31:** 851–2.

Adverse Effects and Treatment

Adverse effects are common with amiodarone. Many are dose-related and reversible with reduction in dose; however, because of its long half-life this can take some time and adverse effects may develop after treatment is stopped.

Adverse cardiovascular effects associated with amiodarone include severe bradycardia, sinus arrest, and conduction disturbances. Severe hypotension may follow intravenous use, particularly (though not exclusively) at rapid infusion rates. Amiodarone may also produce ventricular tachyarrhythmias; torsade de pointes has been reported but appears to be less of a problem with amiodarone than other antiarrhythmics. Rarely, heart failure may be precipitated or aggravated.

Amiodarone reduces the peripheral transformation of thyroxine (T_4) to tri-iodothyronine (T_3) and increases the formation of reverse-T_3. It can affect thyroid function and may induce hypo- or hyperthyroidism.

There have been reports of severe pulmonary toxicity including pulmonary fibrosis and interstitial pneumonitis. These effects are usually reversible on withdrawal of amiodarone but are potentially fatal.

Amiodarone can adversely affect the liver. There may be abnormal liver function tests and cirrhosis or hepatitis; fatalities have been reported.

Prolonged use of amiodarone causes the development of benign yellowish-brown corneal microdeposits in the majority of patients, sometimes associated with coloured haloes of light; these are reversible on stopping therapy. Photosensitivity reactions are also common and more rarely blue-grey discoloration of the skin may occur.