Respiratory-tract disorders. Nebulised adrenaline may be used to reverse airway obstruction in inflammatory disorders such as croup since it relieves inflammation and also causes bronchodilatation. Although some studies in acute viral bronchiolitis (see Respiratory Syncytial Virus Infection, p.860) have shown improvement in clinical scores,[1,2] randomised studies have failed to find any difference in outcome between infants treated with adrenaline and either salbutamol[3] or placebo.[4] A systematic review[5] found insufficient evidence to support the use of adrenaline in inpatients, although there was a suggestion that it might be of short-term benefit in outpatients.

However, the *BNF* states that for severe croup not effectively controlled with corticosteroids, nebulised adrenaline solution 1 in 1000 may be given with close clinical monitoring in a dose of 400 micrograms/kg (up to a maximum of 5 mg) repeated after 30 minutes if necessary. The effects of nebulised adrenaline are expected to last 2 to 3 hours.

There has also been a report[6] of the successful use of nebulised adrenaline in a 15-month-old child with airway inflammation secondary to the ingestion of sodium hypochlorite.

1. Reijonen T, *et al.* The clinical efficacy of nebulized racemic epinephrine and albuterol in acute bronchiolitis. *Arch Pediatr Adolesc Med* 1995; **149:** 686–92.
2. Menon K, *et al.* A randomized trial comparing the efficacy of epinephrine with salbutamol in the treatment of acute bronchiolitis. *J Pediatr* 1995; **126:** 1004–7.
3. Patel H, *et al.* A randomized, controlled trial of the effectiveness of nebulized therapy with epinephrine compared with albuterol and saline in infants hospitalized for acute viral bronchiolitis. *J Pediatr* 2002; **141:** 818–24.
4. Wainwright C, *et al.* A multicenter, randomized, double-blind, controlled trial of nebulized epinephrine in infants with acute bronchiolitis. *N Engl J Med* 2003; **349:** 27–35.
5. Hartling L, *et al.* Epinephrine for bronchiolitis. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 07/10/05).
6. Ziegler D, Bent G. Caustic-induced upper airway obstruction responsiveness to nebulized adrenaline. *Pediatrics* 2001; **107:** 807–8.

Preparations

BP 2008: Adrenaline Eye Drops; Adrenaline Injection; Adrenaline Solution; Bupivacaine and Adrenaline Injection; Dilute Adrenaline Injection I in 10,000; Lidocaine and Adrenaline Injection;
USP 31: Cocaine and Tetracaine Hydrochlorides and Epinephrine Topical Solution; Epinephrine Bitartrate for Ophthalmic Solution; Epinephrine Bitartrate Inhalation Aerosol; Epinephrine Bitartrate Ophthalmic Solution; Epinephrine Inhalation Aerosol; Epinephrine Inhalation Solution; Epinephrine Injection; Epinephrine Nasal Solution; Epinephrine Ophthalmic Solution; Epinephryl Borate Ophthalmic Solution; Lidocaine Hydrochloride and Epinephrine Injection; Prilocaine and Epinephrine Injection; Procaine Hydrochloride and Epinephrine Injection; Racepinephrine Inhalation Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: EpiPen; ***Austral.:*** EpiPen; ***Austria:*** EpiPen; Suprarenin; ***Belg.:*** EpiPen; ***Braz.:*** Drenalin; Nefrin†; ***Canad.:*** EpiPen; Twinject; Vaponefrin; ***Cz.:*** Anapen; EpiPen; Glaucon†; ***Denm.:*** EpiPen; ***Fin.:*** EpiPen; ***Fr.:*** Anahelp; Anapen; ***Ger.:*** Anapen; Fastjekt; InfectoKrupp; Suprarenin; ***Gr.:*** Anapen; EpiPen; ***Hung.:*** Anapen; EpiPen; Tonogen; ***Irl.:*** Anapen; Eppy†; ***Israel:*** EpiPen; ***Ital.:*** Fastjekt; ***Malaysia:*** EpiPen; ***Mex.:*** Pinadrina; ***Neth.:*** EpiPen; ***Norw.:*** EpiPen; ***NZ:*** EpiPen; ***Philipp.:*** Adrenin; ***Pol.:*** Anapen; EpiPen; Fastjekt; ***Port.:*** Anapen; EpiPen; ***S.Afr.:*** Adrenotone; Ana-Guard; EpiPen; Eppy; Simplene; ***Spain:*** Adreject; ***Swed.:*** Anapen; EpiPen; Eppy†; ***Switz.:*** EpiPen; ***UK:*** Anapen; EpiPen; ***USA:*** AsthmaHaler Mist; AsthmaNefrin; Epifrin†; Epinal; EpiPen; Glaucon†; microNefrin; Nephron; Primatene Mist; Primatene Mist Suspension; S-2.

Multi-ingredient: ***Arg.:*** Asmopul†; Yanal; ***Austral.:*** Rectinol; ***Ger.:*** Links-Glaukosan†; Mydrial-Atropin†; ***Hung.:*** Hemorid; Noditran†; ***India:*** Brovon; ***Irl.:*** Ganda; ***Ital.:*** Pilodren†; Rinantipiol†; ***Port.:*** Adrinex†; ***Spain:*** Coliniocilina Adren Astr; Epistaxol; ***Switz.:*** Haemocortin; ***UK:*** Brovon; ***USA:*** Ana-Kit; E-Pilo†; Emergent-Ez; PE†.

Used as an adjunct in: ***Arg.:*** Caina G; Duracaine; Gobbicaina; Larjancaina; Xylocaina; ***Austral.:*** Citanest Dental; Lignospan†; Marcain; Nurocain; Scandonest†; Xylocaine; ***Austria:*** Neo-Xylestesin; Neo-Xylestesin forte; Scandonest; Septanest; Ubistesin; Ultracain Dental; Xylanaest; Xylocain; ***Belg.:*** Citanest; Marcaine; Ubistesin†; Xylocaine; ***Braz.:*** Bupiabbott Plus; Lidocabbott; Lidogeyer†; Marcaina; Neocaina; Novabupi; Xylestesin; Xylocaina; ***Canad.:*** Astracaine†; Citanest†; Marcaine; Sensorcaine; Xylocaine; ***Cz.:*** Marcaine; Scandonest; Septanest S; Supracain; Ubistesin; Ultracain D-S†; Xylestesin-A†; ***Denm.:*** Carbocain; Marcain; Scandonest; Septanest; Septocaine; Ubistesin; Xylocain; Xyloplyin; ***Fin.:*** Marcain; Septocaine; Ubistesin; Ultracain D-Suprarenin; Xylocain; ***Fr.:*** Alphacaine; Marcaine†; Predesic†; Ubistesin Adrenalinee; Xylocaine; ***Ger.:*** Ubistesin; Ultracain D-S; Ultracain Suprarenin; Xylestesin-A, Xylestesin centro†; Xylestesin-S†; Xylocain; Xylocitin; Xylonest; ***Gr.:*** Marcaine; Xylocaine; ***Hong Kong:*** Marcain; Ubistesin; Xylestesin-A; Xylocaine; ***Hung.:*** Ubistesin; Ultracain D-S; ***India:*** Gesicain; Xylocaine; ***Indon.:*** Extracaine; Pehacain; ***Irl.:*** Marcain; Xylocaine; ***Israel:*** Kamacaine; Lidocadren†; Marcaine; ***Ital.:*** Alfacaina; Bupicain; Bupiforan; Bupisen; Bupisolver; Bupixamol; Carbocaina; Carbosen; Cartidont; Citocartin; Ecocain; Lident Adrenalina†; Lident Andrenor†; Marcaina; Mepi-Mynol; Mepicain; Mepident; Mepiforan; Mepisolver; Mepivamol; Molcain†; Optocain; Primacaine†; Sarticain; Scandonest; Septanest; Ubistesin; Xilo-Mynol; Xylonor; Xyloplyina; ***Malaysia:*** Denkan; Marcain; ***Mex.:*** Buvacaina; Pisacaina; Unicaine; Xylocaina; ***Neth.:*** Bupiforan; Citanest; Lignospan; Marcaine; Scandicaine; Septanest; Ubistesin; Ultracain D-S; Xylocaine; ***Norw.:*** Marcain; Septocaine; Xylocain; ***NZ:*** Marcain; Septanest; Topicaine; Xylestesin-A; Xylocaine; ***Philipp.:*** Dentocaine; ***Pol.:*** Marcaine; ***Port.:*** Alphacaine; Artinibsa; Artinostrum; Bupinostrum; Lidonostrum; Lincaina; Meganest; Octocaine; Scandinibsa; Septanest; Ubistesin; Xilonibsa; ***Rus.:*** Ultracain (Ультракаин); ***S.Afr.:*** Lignospan Special†; Macaine; Scandonest†; Xylotox; ***Singapore:*** Xylocaine; ***Spain:*** Anestesia Topi Braun C/A; Articaina C/E; Meganest; Octocaine; Scandinibsa; Ultracain; Xilonibsa; Xylonor Especial; ***Swed.:*** Carbocain; Marcain; Xylocain; ***Switz.:*** Alphacaine; Carbostesin; Lignospan†; Rapidocaine; Rudocaine; Scandonest; Septanest; Ubistesin; Ultracaine D-S; Xylestesin-S "special"†; Xylocain; Xylonest; Xyloplyin†; ***Thai.:*** Lidocation; Lidocaton†; Xylocaine; ***Turk.:*** Jetokain; Jetosel; Ultracain; ***UAE:*** Ecocain; ***UK:*** Lignostab-A†; Septanest; Xylocaine; Xylotox†; ***USA:*** Citanest; Duranest†; Marcaine; Octocaine; Sensorcaine; Septocaine; Xylocaine.

Ajmaline

Aimaliini; Ajmalin; Ajmalina; Ajmalinum; Rauwolfine. (17*R*,21*R*)-Ajmalan-17,21-diol.

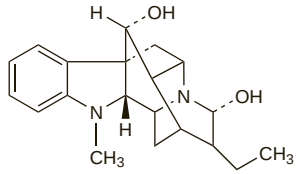
Аймалин

$C_{20}H_{26}N_2O_2$ = 326.4.

CAS — 4360-12-7.

ATC — C01BA05.

ATC Vet — QC01BA05.



Pharmacopoeias. In *Jpn.*

Adverse Effects

Ajmaline depresses the conductivity of the heart, and at high doses can cause heart block. At very high doses it may produce a negative inotropic effect. High doses may cause cardiac arrhythmias, coma, and death. Arrhythmias have also been reported after usual intravenous doses (see below). Adverse neurological effects have been reported including eye twitching, convulsions, and respiratory depression. Hepatotoxicity and agranulocytosis may occasionally occur.

Effects on the heart. Electrophysiologic study[1] in 1955 patients revealed that ajmaline 1 mg/kg given intravenously could induce arrhythmias; 63 developed a supraventricular arrhythmia and 7 an atrioventricular re-entrant tachycardia. Ventricular tachycardia[2,3] and torsade de pointes[4] have been reported during diagnostic use.

1. Brembilla-Perrot B, Terrier de la Chaise A. Provocation of supraventricular tachycardias by an intravenous class I antiarrhythmic drug. *Int J Cardiol* 1992; **34:** 189–98.
2. Rolf S, *et al.* The ajmaline challenge in Brugada syndrome: diagnostic impact, safety, and recommended protocol. *Eur Heart J* 2003; **24:** 1104–12.
3. Pinar Bermúdez E, *et al.* Spontaneous sustained monomorphic ventricular tachycardia after administration of ajmaline in a patient with Brugada syndrome. *Pacing Clin Electrophysiol* 2000; **23:** 407–9.
4. Haverkamp W, *et al.* Torsade de pointes induced by ajmaline. *Z Kardiol* 2001; **90:** 586–90.

Precautions

As for Quinidine, p.1384.

Interactions

Antiarrhythmics. Oral use of *quinidine* with ajmaline increased plasma concentrations of ajmaline considerably in 4 healthy subjects; the elimination half-life of ajmaline was increased about twofold.[1] The pharmacokinetics of quinidine did not seem to be affected by ajmaline.

1. Hori R, *et al.* Quinidine-induced rise in ajmaline plasma concentration. *J Pharm Pharmacol* 1984; **36:** 202–4.

Uses and Administration

Ajmaline is an alkaloid obtained from the root of *Rauwolfia serpentina* (Apocynaceae). It is a class Ia antiarrhythmic (p.1153) used in the treatment of supraventricular and ventricular arrhythmias (p.1160) and for differential diagnosis of Wolff-Parkinson-White syndrome. Ajmaline is given by intravenous injection in a usual dose of 50 mg over at least 5 minutes. It may also be given by intravenous infusion, and has been given orally and by intramuscular injection.

Ajmaline has also been used as the hydrochloride, monoethanolate, and phenobarbital salts.

Brugada syndrome. Brugada syndrome is a congenital disorder affecting myocardial sodium channels and may be associated with sudden cardiac death. Class 1a antiarrhythmics such as ajmaline block the sodium channel and may have a role in the diagnosis of Brugada syndrome, although they are not suitable for treatment.

References.

1. Rolf S, *et al.*The ajmaline challenge in Brugada syndrome: diagnostic impact, safety, and recommended protocol. *Eur Heart J* 2003; **24:** 1104–12.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Gilurytmal; ***Cz.:*** Gilurytmal†; ***Ger.:*** Gilurytmal.

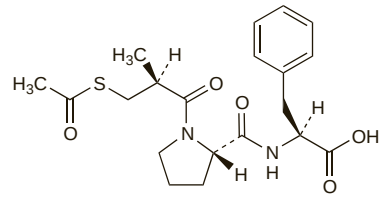
Alacepril *(rINN)*

Alacépril; Alaceprilum; DU-1219. *N*-{1-[(*S*)-3-Mercapto-2-methylpropionyl]-L-prolyl}-3-phenyl-L-alanine acetate.

Алацеприл

$C_{20}H_{26}N_2O_5S$ = 406.5.

CAS — 74258-86-9.



Pharmacopoeias. In *Jpn.*

Profile

Alacepril is an ACE inhibitor (p.1193) used in the treatment of hypertension (p.1171). It is converted to captopril and desacetylalacepril (DU-1227) in the body after oral doses. It is given orally in a usual dose of 25 to 75 mg daily, as a single dose or in two divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Cetapril.

Aliskiren Fumarate *(USAN, rINNM)*

Aliskiren Hemifumarate; Aliskirène, Fumarate de; Aliskireni Fumaras; CGP-60536B; Fumarato de aliskireno; SPP-100 (aliskiren or aliskiren fumarate). Bis(2*S*,4*S*,5*S*,7*S*)-5-amino-*N*-(2-carbamoyl-2-methylpropyl)-4-hydroxy-2-isopropyl-7-[4-methoxy-3-(3-methoxypropoxy)benzyl]-8-methylnonanamide fumarate (2:1).

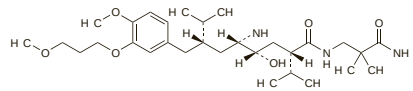
Алискирена Фумарат

$(C_{30}H_{53}N_3O_6)_2,C_4H_4O_4$ = 1219.6.

CAS — 173334-57-1 (aliskiren); 173334-58-2 (aliskiren fumarate).

ATC — C09XA02.

ATC Vet — QC09XA02.



(aliskiren)

Adverse Effects and Precautions

Aliskiren is generally well-tolerated but may produce dose-related gastrointestinal adverse effects including diarrhoea, abdominal pain, dyspepsia, and gastro-oesophageal reflux. Other adverse effects include hypotension, headache, dizziness, fatigue, back pain, and cough; rashes, hyperuricaemia, gout, and renal calculi may also occur. Angioedema has been reported rarely, and there have also been reports of seizures. As with other inhibitors of the renin-angiotensin system, dose-related decreases in haemoglobin have been reported.

Aliskiren should be avoided in pregnancy since drugs acting on the renin-angiotensin system have been associated with fetal and neonatal morbidity and mortality. It should be used with caution in patients with renal impairment or renovascular hypertension. Patients with sodium or volume depletion (for example those receiving high-dose diuretics) may experience symptomatic hypotension on starting aliskiren and treatment should begin under close medical supervision.

Interactions

Use of aliskiren with other antihypertensives or drugs that cause hypotension may have an additive effect. Renal function and electrolytes should be monitored in diabetic patients taking aliskiren and ACE inhibitors since there is an increased risk of hyperkalaemia and renal impairment.