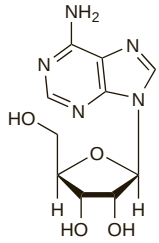
Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Olbetam; ***Belg.:*** Olbetam; ***Braz.:*** Olbetam†; ***Chile:*** Olbetam; ***Denm.:*** Olbetam; ***Ger.:*** Olbemox†; ***Gr.:*** Olbetam; ***Hong Kong:*** Olbetam; ***Hung.:*** Olbetam; ***Irl.:*** Olbetam†; ***Israel:*** Olbetam; ***Ital.:*** Olbetam; ***Mex.:*** Olbetam†; ***Neth.:*** Nedios; Olbetam; ***NZ:*** Olbetam; ***S.Afr.:*** Olbetam; ***Singapore:*** Olbetam; ***Switz.:*** Olbetam; ***Thai.:*** Olbetam; ***UK:*** Olbetam.

Adenosine *(BAN, USAN)*

Adenocin; Adenosiini; Adenosin; Adenosina; Adénosine; Adenosinum; Adenozin; Adenozinas; Adenozyna; SR-96225; SUNY-4001. 6-Amino-9-β-D-ribofuranosyl-9*H*-purine.

Аденозин
$C_{10}H_{13}N_5O_4$ = 267.2.
CAS — 58-61-7.
ATC — C01EB10.
ATC Vet — QC01EB10.



Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Adenosine). A white, or almost white, crystalline powder. Slightly soluble in water; soluble in hot water; practically insoluble in alcohol and in dichloromethane; dissolves in dilute mineral acids.
USP 31 (Adenosine). A white, odourless crystalline powder. Slightly soluble in water; practically insoluble in alcohol. Store in airtight containers. Protect from light.

Stability. Adenosine was found to be stable[1] when it was mixed with glucose 5%, lactated Ringer's, sodium chloride 0.9%, or a mixture of glucose 5% and lactated Ringer's and stored in polypropylene syringes or PVC bags.

1. Ketkar VA, *et al.* Stability of undiluted and diluted adenosine at three temperatures in syringes and bags. *Am J Health-Syst Pharm* 1998; **55:** 466–70.

Adverse Effects, Treatment, and Precautions

Adverse effects of adenosine are usually transient, lasting less than a minute, due to its very short plasma half-life. They include nausea, lightheadedness, flushing, headache, angina-like chest pain, apprehension, and dyspnoea. Bronchospasm has been reported. Like other antiarrhythmics, adenosine may worsen arrhythmias. Bradycardia and heart block have been reported. Adenosine is a vasodilator and reduces blood pressure; the larger doses given by intravenous infusion may rarely produce significant hypotension and reflex tachycardia. Infusion may also be associated with abdominal, throat, neck, and jaw discomfort. Treatment is rarely needed for adverse effects but in persistent cases aminophylline or theophylline may be given.

Adenosine is contra-indicated in patients with second- or third-degree AV block or in those with sick sinus syndrome (unless they have a pacemaker) and should be avoided or used with caution in patients with QT prolongation since torsade de pointes has occurred very rarely. It is also contra-indicated in asthmatic subjects and should be used with caution in patients with obstructive pulmonary disease. Intravenous infusion of adenosine should be used with caution in patients who may develop hypotensive complications such as those with autonomic dysfunction, pericarditis, or stenotic valvular heart disease. Patients with recent heart transplantation may have increased sensitivity to the cardiac effects of adenosine.

◊ Use of the *University of Wisconsin solution* [UW Solution; Belzer UW Solution (commercially available as *Viaspan*)] for the hypothermic storage of kidneys before transplantation has been associated with bradycardia, prolonged PR intervals, and heart block.[1,2] The solution contains hetastarch, allopurinol, glutathione, and adenosine. The adenosine was considered to be the arrhythmogenic factor. Some centres had used the solution to flush kidneys before implantation,[2] a use for which it was never intended.[3] When used properly the adenosine in solution is catabolised to hypoxanthine and inosine, which do not cause cardiac problems, but this takes some time in hypothermic conditions.[3]

1. Prien T, *et al.* Bradyarrhythmia with University of Wisconsin preservation solution. *Lancet* 1989; **i:** 1319–20.
2. Vanrenterghem Y, *et al.* University of Wisconsin preservation solute and bradyarrhythmia. *Lancet* 1989; **ii:** 745.
3. Belzer FO. Correct use of University of Wisconsin preservation solution. *Lancet* 1990; **335:** 362.

Effects on the heart. Like most antiarrhythmics, adenosine can worsen arrhythmias, and both bradyarrhythmias and tachyarrhythmias have been reported.[1] Atrial fibrillation may develop in patients given adenosine for paroxysmal supraventricular tachycardia, and in a prospective study[2] occurred in 12% of 200 patients. Although most arrhythmias are of minor importance, ventricular arrhythmias and haemodynamic compromise have been reported[3,4] in patients given adenosine for presumed supraventricular tachycardia who were later discovered to have Wolff-Parkinson-White syndrome. Fatal cardiac arrest has also occurred[5] after the use of adenosine for arrhythmias in 2 patients with underlying cardiopulmonary disorders.

There have also been reports[6,7] of myocardial infarction in patients with ischaemic heart disease given adenosine during stress imaging.

For arrhythmias associated with the use of adenosine in organ preservation solutions see above.

1. Mallet ML. Proarrhythmic effects of adenosine: a review of the literature. *Emerg Med J* 2004; **21:** 408–10.
2. Strickberger SA, *et al.* Adenosine-induced atrial arrhythmia: a prospective analysis. *Ann Intern Med* 1997; **127:** 417–22.
3. Exner DV, *et al.* Proarrhythmia in patients with the Wolff-Parkinson-White syndrome after standard doses of intravenous adenosine. *Ann Intern Med* 1995; **122:** 351–2.
4. Nagappan R, *et al.* Potential dangers of the Valsalva maneuver and adenosine in paroxysmal supraventricular tachycardia—beware preexcitation. *Crit Care Resusc* 2002; **4:** 107–11.
5. Haynes BE. Two deaths after prehospital use of adenosine. *J Emerg Med* 2001; **21:** 151–4.
6. Polad JE, Wilson LM. Myocardial infarction during adenosine stress test. Abstract: *Heart* 2002; **87:** 106. Full version: http://heart.bmj.com/cgi/reprint/87/2/e2.pdf (accessed 10/07/07)
7. Reyes E, *et al.* Acute myocardial infarction during adenosine myocardial perfusion imaging. *J Nucl Cardiol* 2004; **11:** 97–9.

Effects on the respiratory system. Acute exacerbation of asthma can be provoked by inhalation of adenosine. Bronchospasm has also been reported in patients with asthma[1,2] or a history of asthma[3] given adenosine intravenously and bronchospasm followed by respiratory failure in a patient with obstructive pulmonary disease.[4] Respiratory arrest has also been reported in an asthmatic patient.[5]

1. DeGroff CG, Silka MJ. Bronchospasm after intravenous administration of adenosine in a patient with asthma. *J Pediatr* 1994; **125:** 822–3.
2. Drake I, *et al.* Bronchospasm induced by intravenous adenosine. *Hum Exp Toxicol* 1994; **13:** 263–5.
3. Hintringer F, *et al.* Supraventricular tachycardia. *N Engl J Med* 1995; **333:** 323.
4. Burkhart KK. Respiratory failure following adenosine administration. *Am J Emerg Med* 1993; **11:** 249–50.
5. Patton JW, Sharma GK. Adenosine-induced respiratory arrest in an asthmatic patient. *South Med J* 2008; **101:** 328–9.

Migraine. A 35-year-old man with a history of migraine developed symptoms identical to those of his usual episodes of migraine immediately after 2 intravenous bolus doses of adenosine.[1]

1. Brown SGA, Waterer GW. Migraine precipitated by adenosine. *Med J Aust* 1995; **162:** 389–91.

Interactions

Dipyridamole inhibits adenosine uptake and therefore may potentiate the action of adenosine; if use of the two drugs is essential the dosage of adenosine should be reduced. Theophylline and other xanthines are competitive antagonists of adenosine. The risk of AV block may be increased if adenosine is used with other drugs that slow AV conduction.

Pharmacokinetics

Intravenous adenosine is rapidly taken up by an active transport system into erythrocytes and vascular endothelial cells where it is metabolised to inosine and adenosine monophosphate. The plasma half-life is less than 10 seconds.

Uses and Administration

Adenosine is an endogenous adenine nucleoside that is one of the components of nucleic acids (p.2355) and many coenzymes; as such, it is involved in many biological processes. It acts as an antiarrhythmic by stimulating adenosine A_1-receptors and slowing conduction through the AV node. It does not fit into the usual classification of antiarrhythmics (p.1153). It also produces peripheral and coronary vasodilatation by stimulating adenosine A_2-receptors.

Adenosine is used to restore sinus rhythm in the treatment of paroxysmal supraventricular tachycardia, including that associated with the Wolff-Parkinson-White syndrome (but see Effects on the Heart, above). It is also used for the differential diagnosis of broad or narrow complex supraventricular tachycardias and in myocardial imaging.

In the treatment of **paroxysmal supraventricular tachycardia**, adenosine may be given in an initial dose of 3 mg by rapid intravenous injection. If this dose is not effective within 1 to 2 minutes, 6 mg may be given and if necessary, 12 mg after a further 1 to 2 minutes. Alternatively, an initial dose of 6 mg followed if necessary by two further doses of 12 mg at 1 to 2 minute intervals may be used, but this higher initial dose should not be given to heart transplant patients as they have an increased sensitivity to adenosine. For differential **diagnosis of supraventricular tachycardias** a similar dosage regimen is used, beginning with a dose of 3 mg followed by 6 mg and then 12 mg at 1 to 2 minute intervals if required. Doses for children with paroxysmal supraventricular tachycardia are discussed below.

In **myocardial imaging** adenosine is given by intravenous infusion in a dose of 140 micrograms/kg per minute for 6 minutes. The radionuclide is injected after 3 minutes of the infusion.

Adenosine and its derivatives, such as adenosine phosphate (p.2247) and adenosine triphosphate (p.2247), have been used in various metabolic disorders because of their role in biological processes. Adenosine triphosphate, as the disodium salt, has been used as an antiarrhythmic.

Administration in children. Adenosine may be used for the management of paroxysmal supraventricular tachycardia in children. Dosage recommendations vary. Licensed product information in the USA states that children weighing less than 50 kg, including neonates and infants, may be given an initial dose of 50 to 100 micrograms/kg; if this is not effective the dose may be increased by 50 to 100 micrograms/kg increments at 1 to 2 minute intervals until the arrhythmia is controlled or a single dose of 300 micrograms/kg is reached. Paediatric advanced cardiac life support guidelines[1] in the USA recommend an initial dose of 100 micrograms/kg (maximum 6 mg) followed by a second dose of 200 micrograms/kg (maximum 12 mg) if required, and are applicable to infants and children. In the UK, the BNFC recommends an initial dose of 100 micrograms/kg for children aged 1 to 12 years, or 150 micrograms/kg for neonates and infants up to 1 year; the dose may be increased by increments of 50 to 100 micrograms/kg at 2 minute intervals, to a maximum single dose of 300 micrograms/kg for neonates and 500 micrograms/kg for infants and children.

1. The American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 12: pediatric advanced life support. *Circulation* 2005; **112:** (suppl 1): IV167–IV187. Also available at: http://circ.ahajournals.org/cgi/reprint/112/24_suppl/IV-167 (accessed 10/07/07)

Cardiac arrhythmias. Adenosine is used for the termination of paroxysmal supraventricular tachycardia[1-4] (p.1160) and may often be the drug of choice. Bolus intravenous injection of adenosine produces a rapid response and the extremely short plasma half-life (less than 10 seconds) allows dosage titration every 1 to 2 minutes so that most episodes can be controlled within 5 minutes without the danger of drug accumulation.

Adenosine has been used successfully in pregnant women with paroxysmal supraventricular tachycardia[5-8] and cardioversion of fetal supraventricular tachycardia by direct fetal therapy with adenosine has been reported.[9,10]

Adenosine can be used for the differential **diagnosis** of broad complex tachycardia where the mechanism is not known.[1] If the cause is supraventricular, adenosine will terminate the arrhythmia or produce AV block to reveal the underlying atrial rhythm. If the cause is ventricular, adenosine will have no effect on the tachycardia, whereas if an alternative treatment such as verapamil is given to these patients severe hypotension and cardiac arrest can occur.

1. Faulds D, *et al.* Adenosine: an evaluation of its use in cardiac diagnostic procedures, and in the treatment of paroxysmal supraventricular tachycardia. *Drugs* 1991; **41:** 596–624.
2. Garratt CJ, *et al.* Adenosine and cardiac arrhythmias. *BMJ* 1992; **305:** 3–4.
3. Rankin AC, *et al.* Adenosine and the treatment of supraventricular tachycardia. *Am J Med* 1992; **92:** 655–64.

4. Anonymous. Adenosine for acute cardiac arrhythmias. *Drug Ther Bull* 1993; **31:** 49–50.
5. Mason BA, *et al.* Adenosine in the treatment of maternal paroxysmal supraventricular tachycardia. *Obstet Gynecol* 1992; **80:** 478–80.
6. Afridi I, *et al.* Termination of supraventricular tachycardia with intravenous adenosine in a pregnant woman with Wolff-Parkinson-White syndrome. *Obstet Gynecol* 1992; **80:** 481–3.
7. Hagley MT, Cole PL. Adenosine use in pregnant women with supraventricular tachycardia. *Ann Pharmacother* 1994; **28:** 1241–2.
8. Hagley MT, *et al.* Adenosine use in a pregnant patient with supraventricular tachycardia. *Ann Pharmacother* 1995; **29:** 938.
9. Blanch G, *et al.* Cardioversion of fetal tachyarrhythmia with adenosine. *Lancet* 1994; **344:** 1646.
10. Kohl T, *et al.* Direct fetal administration of adenosine for the termination of incessant supraventricular tachycardia. *Obstet Gynecol* 1995; **85:** 873–4.

Ischaemic heart disease. Adenosine produces coronary vasodilatation and may be used to provide a pharmacological stress in patients undergoing assessment of their ischaemic heart disease when exercise stress is inappropriate.[1] It has been used with radionuclide imaging, echocardiography, and magnetic resonance imaging.

Adenosine has also been tried as an adjunct to prevent reperfusion injury in the management of acute myocardial infarction. Improved coronary blood flow has been reported[2] with intracoronary adenosine, and both intracoronary[3] and intravenous[4] adenosine have reduced infarct size, but no improvement in clinical outcomes has been shown.[5-7] A reduction in myonecrosis has also been reported[8] with intracoronary adenosine given at the start of non-urgent percutaneous coronary interventions.

1. Ali Raza J, *et al.* Pharmacological stress agents for evaluation of ischemic heart disease. *Int J Cardiol* 2001; **81:** 157–67.
2. Vijayalakshmi K, *et al.* Prospective, randomised, controlled trial to study the effect of intracoronary injection of verapamil and adenosine on coronary blood flow during percutaneous coronary intervention in patients with acute coronary syndromes. *Heart* 2006; **92:** 1278–84.
3. Claeys MJ, *et al.* Effect of intracoronary adenosine infusion during coronary intervention on myocardial reperfusion injury in patients with acute myocardial infarction. *Am J Cardiol* 2004; **94:** 9–13.
4. Mahaffey KW, *et al.* Adenosine as an adjunct to thrombolytic therapy for acute myocardial infarction: results of a multicenter, randomized, placebo-controlled trial: the Acute Myocardial Infarction STudy of ADenosine (AMISTAD) trial. *J Am Coll Cardiol* 1999; **34:** 1711–20.
5. Ross AM, *et al.* A randomized, double-blinded, placebo-controlled multicenter trial of adenosine as an adjunct to reperfusion in the treatment of acute myocardial infarction (AMISTAD-II). *J Am Coll Cardiol* 2005; **45:** 1775–80.
6. Quintana M, *et al.* Left ventricular function and cardiovascular events following adjuvant therapy with adenosine in acute myocardial infarction treated with thrombolysis: results of the ATTenuation by Adenosine of Cardiac Complications (ATTACC) study. *Eur J Clin Pharmacol* 2003; **59:** 1–9.
7. Petronio AS, *et al.* Left ventricular remodeling after primary coronary angioplasty in patients treated with abciximab or intracoronary adenosine. *Am Heart J* 2005; **150:** 1015. Full version: http://download.journals.elsevierhealth.com/pdfs/journals/0002-8703/PIIS0002870305007313.pdf (accessed 26/06/07)
8. Lee C-H, *et al.* Pretreatment with intracoronary adenosine reduces the incidence of myonecrosis after non-urgent percutaneous coronary intervention: a prospective randomized study. *Eur Heart J* 2007; **28:** 19–25.

Pain. Adenosine receptors are present in the CNS and there is some evidence[1,2] that adenosine, given intravenously or intrathecally, may have an analgesic effect.

1. Hayashida M, *et al.* Clinical application of adenosine and ATP for pain control. *J Anesth* 2005; **19:** 225–35.
2. Gan TJ, Habib AS. Adenosine as a non-opioid analgesic in the perioperative setting. *Anesth Analg* 2007; **105:** 487–94.

Pulmonary hypertension. Vasodilators have been tried in persistent pulmonary hypertension of the newborn (p.1179), but their use is generally restricted by lack of selectivity for the pulmonary circulation. A randomised placebo-controlled study[1] in 18 term infants with persistent pulmonary hypertension indicated that intravenous infusion of adenosine improved oxygenation without causing hypotension or tachycardia; however, the study was too small to assess any effect on mortality and/or the need for extracorporeal membrane oxygenation. Another observational study[2] in neonates with an inadequate response to inhaled nitric oxide suggested that addition of adenosine infusion also improved oxygenation.

1. Konduri GG, *et al.* Adenosine infusion improves oxygenation in term infants with respiratory failure. *Pediatrics* 1996; **97:** 295–300.
2. Ng C, *et al.* Adenosine infusion for the management of persistent pulmonary hypertension of the newborn. *Pediatr Crit Care Med* 2004; **5:** 10–13.

Preparations

USP 31: Adenosine Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Euritsin†; ***Austral.:*** Adenocor; Adenoscan; ***Austria:*** Adenoscan; Adrekar; ***Belg.:*** Adenocor; ***Braz.:*** Adenocard; ***Canad.:*** Adenocard; ***Chile:*** Tricor; ***Cz.:*** Adenocor; Adenoscan†; ***Denm.:*** Adenocor; ***Fin.:*** Adenocor; Adenoscan†; ***Fr.:*** Adenoscan; Krenosin; ***Ger.:*** Adenoscan; Adrekar; ***Gr.:*** Adenocor; ***Hong Kong:*** Adenoscan; ***Hung.:*** Adenocor; ***India:*** Adenoject; ***Irl.:*** Adenocor; ***Israel:*** Adenocor; ***Ital.:*** Adenoscan; Krenosin; ***Jpn:*** Adenoscan; ***Malaysia:*** Adenocor; ***Mex.:*** Krenosin; ***Neth.:*** Adenocor; Adenoscan; ***Norw.:*** Adenocor; ***NZ:*** Adenocor; ***Philipp.:*** Cardiovert; ***Pol.:*** Adenocor; ***Rus.:*** Vita-Iodurol (Вита-иодурол); ***S.Afr.:*** Adenocor; ***Singapore:*** Adenocor; ***Spain:*** Adenocor; Adenoscan; ***Switz.:*** Krenosine; ***Thai.:*** Adenocor; ***UK:*** Adenocor; Adenoscan; ***USA:*** Adenocard; Adenoscan; ***Venez.:*** Adenocor†.

Multi-ingredient: *Belg.:* Vitacic; ***Braz.:*** Aminotox†; Anekron; Betaliver†; Biohepax; Enterofigon; Epativan; Epocler; Hepacitron†; Hepatobe†; Hepatox; Hormo Hepatico†; Necro B-6; ***Cz.:*** Laevadosin†; ***Hung.:*** Vitacic†; ***Mon.:*** Vitacic; ***Philipp.:*** Godex; ***Rus.:*** Oftan Catachrom (Офтан Катахром); Vitacic (Витасик)†; ***Spain:*** Vitaphakol.

Adrenaline *(BAN)* ⊗

Epinephrine *(BAN, rINN)*; Adrenaliini; Adrenalin; Adrenalina; Adrénaline; Adrenalinum; Epinefriini; Epinefrin; Epinefrina; Epinefryna; Épinéphrine; Epinephrinum; Epirenamine; Levorenin; Suprarenin. (*R*)-1-(3,4-Dihydroxyphenyl)-2-methylaminoethanol.

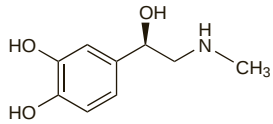
Эпинефрин

$C_9H_{13}NO_3$ = 183.2.

CAS — 51-43-4.

ATC — A01AD01; B02BC09; C01CA24; R01AA14; R03AA01; S01EA01.

ATC Vet — QA01AD01; QB02BC09; QC01CA24; QR01AA14; QR03AA01; QS01EA01.



NOTE. Endogenous adrenaline and the monograph substance are the laevo-isomer.
ADN and EPN are codes approved by the BP 2008 for use on single unit doses of eye drops containing adrenaline where the individual container may be too small to bear all the appropriate labelling information.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet*.
US also includes the racemic substances Racepinephrine (Racepinefrine (*rINN*)) and Racepinephrine Hydrochloride (Racepinefrine Hydrochloride (*rINNM*)).
Ph. Eur. 6.2 (Adrenaline). A white or almost white crystalline powder, becoming coloured on exposure to air and light. Practically insoluble in water, in alcohol, and in dichloromethane. It dissolves in hydrochloric acid. Store under nitrogen. Protect from light.
USP 31 (Epinephrine). A white to practically white, odourless, microcrystalline powder or granules, gradually darkening on exposure to light and air. With acids, it forms salts that are readily soluble in water, and the base may be recovered by the addition of ammonia water or alkali carbonates. Very slightly soluble in water and in alcohol; insoluble in chloroform, in ether, and in fixed and volatile oils. Solutions are alkaline to litmus. Store in airtight containers. Protect from light.

Adrenaline Acid Tartrate *(BANM)* ⊗

Epinephrine Bitartrate *(rINNM)*; Adrenaliinitartraatti; Adrenaline Bitartrate; Adrenaline Tartrate; Adrénaline, Tartrate d'; Adrenalini Bitartras; Adrenalini tartras; Adrenalinii Tartras; Adrenalinium Hydrogentartaricum; Adrenalino tartratas; Adrenalin-tartarát; Adrenalintartrat; Bitartrato de epinefrina; Epinefrin-tartarát; Epinefryny wodorowinian; Epinephrine Acid Tartrate *(BANM)*; Épinéphrine, Bitartrate d'; Epinephrine Hydrogen Tartrate; Epinephrini Bitartras; Epinephrini Tartras; Epirenamine Bitartrate.

Эпинефрина Битартрат

$C_9H_{13}NO_3,C_4H_6O_6$ = 333.3.

CAS — 51-42-3.

ATC — A01AD01; B02BC09; C01CA24; R01AA14; R03AA01; S01EA01.

ATC Vet — QA01AD01; QB02BC09; QC01CA24; QR01AA14; QR03AA01; QS01EA01.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *US*, and *Viet*.
Ph. Eur. 6.2 (Adrenaline Tartrate; Adrenaline Acid Tartrate BP 2008; Epinephrine Acid Tartrate BP 2008). A white to greyish-white, crystalline powder. Freely soluble in water; slightly soluble in alcohol. Store in airtight containers, or preferably in a sealed tube under vacuum or under an inert gas. Protect from light.
USP 31 (Epinephrine Bitartrate). A white, or greyish-white or light brownish-grey, odourless, crystalline powder. It slowly darkens on exposure to air and light. Soluble 1 in 3 of water; slightly soluble in alcohol; practically insoluble in chloroform and in ether. Its solutions in water are acid to litmus, having a pH of about 3.5. Store in airtight containers. Protect from light.

Stability. Studies on the stability of adrenaline injections.

1. Taylor JB, *et al.* Effect of sodium metabisulphite and anaerobic processing conditions on the oxidative degradation of adrenaline injection BP [1980]. *Pharm J* 1984; **232:** 646–8.
2. Stepensky D *et al.* Long-term stability study of -adrenaline injections: kinetics of sulfonation and racemization pathways of drug degradation. *J Pharm Sci* 2004; **93:** 969–80.

Adrenaline Hydrochloride *(BANM)* ⊗

Epinephrine Hydrochloride *(BANM, rINNM)*; Adrenalin Hidroklorür; Épinéphrine, Chlorhydrate d'; Epinephrini Hydrochloridum; Hidrocloruro de epinefrina.

Эпинефрина Гидрохлорид

$C_9H_{13}NO_3$,HCl = 219.7.

CAS — 55-31-2.

ATC — A01AD01; B02BC09; C01CA24; R01AA14; R03AA01; S01EA01.

ATC Vet — QA01AD01; QB02BC09; QC01CA24; QR01AA14; QR03AA01; QS01EA01.

Adverse Effects

Adrenaline is a potent sympathomimetic and may exhibit the adverse effects typical of both alpha- and beta-adrenoceptor stimulation (see p.1407). Adverse effects such as anxiety, dyspnoea, hyperglycaemia, restlessness, palpitations, tachycardia (sometimes with anginal pain), tremors, sweating, hypersalivation, weakness, dizziness, headache, and coldness of extremities may occur even with low doses. Since adrenaline does not readily cross the blood-brain barrier, its central effects may be largely a somatic response to its peripheral effects. Overdosage may cause cardiac arrhythmias and a sharp rise in blood pressure (sometimes leading to cerebral haemorrhage and pulmonary oedema); these effects may occur at normal dosage in susceptible subjects.

Adrenaline is a potent vasoconstrictor and gangrene may occur if adrenaline-containing local anaesthetic solutions are infiltrated into digits. Extravasation of parenteral adrenaline also results in intense vasoconstriction, leading to tissue necrosis and sloughing. Topical application of adrenaline to mucosal surfaces similarly causes vasoconstriction, which may induce hypoxia leading to compensatory rebound congestion of the mucosa. Inhalation of adrenaline has been associated with epigastric pain, which has been attributed to ingestion of some of the inhalation; it can be minimised by rinsing the mouth and throat with water after inhaling.

Adrenaline eye drops may produce severe smarting, blurred vision, and photophobia on instillation; they may also leave melanin-like deposits in the cornea and conjunctiva, and this has led to obstruction of the nasolachrymal ducts. Repeated use may cause oedema, hyperaemia, and inflammation of the eyes.

Effects on the eyes. In addition to the possibility of pigment deposition and local pain (see above) adrenaline eye drops have been associated with maculopathy, particularly in aphakic eyes (those devoid of a lens).[1] In one report,[2] maculopathy was noted in 15 patients over a period of 4 years; the patients were using adrenaline eye drops containing the hydrochloride, acid tartrate, or adrenaline borate complex (epinephryl borate). Blurring and distortion of vision were followed by decreased visual acuity, and by the appearance of oedema and sometimes haemorrhage in the macular region. A few patients developed cysts near the fovea. These effects appeared within a few weeks of, or several months after, starting therapy and were usually reversible. All except 1 of the patients were aphakic, and retrospective studies have suggested that the incidence of this complication may be up to 30% in aphakic patients.[1,2]

1. Classé JG. Epinephrine maculopathy. *J Am Optom Assoc* 1980; **51:** 1091–3.
2. Kolker AE, Becker B. Epinephrine maculopathy. *Arch Ophthalmol* 1968; **79:** 552–62.

Overdosage. Solutions of racepinefrine for nebulisation have inadvertently been given intravenously, resulting in severe overdosage of adrenaline. A 13-month-old infant[1] was given the equivalent of about 327 micrograms/kg of laevo-adrenaline. Marked pallor, pulselessness, and profound bradycardia developed, but the child responded to cardiopulmonary resuscitation and was subsequently discharged with no evidence of long-term sequelae. However, a 2-year-old child[2] given the equivalent of about 1800 micrograms/kg developed hypertension, tachycardia, and pulmonary oedema, followed by hypotension and subsequent renal failure, requiring transplantation. Subcutaneous overdosage with laevo-adrenaline in another child[3] led to arrhythmias and myocardial ischaemia, and there has also been a report[4] of myocardial infarction and acute renal failure in an adult after injection of the solution from an adrenaline inhaler.

1. Kurachek SC, Rockoff MA. Inadvertent intravenous administration of racemic epinephrine. *JAMA* 1985; **253:** 1441–2.