Breast feeding. Atenolol is distributed into breast milk and there has been a report of cyanosis and bradycardia in a breast-fed neonate whose mother had been taking atenolol (see under Pharmacokinetics, below). The American Academy of Pediatrics therefore considers[1] that it should be given with caution to breast-feeding mothers.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 10/01/08)

Effects on the eyes. Visual symptoms without headache were associated with atenolol for migraine prophylaxis in a patient who had experienced a similar reaction with nadolol.[1]

1. Kumar KL, Cooney TG. Visual symptoms after atenolol therapy for migraine. *Ann Intern Med* 1990; **112:** 712–13. Correction. *ibid.*; **113:** 257.

Effects on the heart. Beta blockers are used in the management of cardiac arrhythmias. However, atenolol 2.5 mg by intravenous injection induced atrial fibrillation in 6 of 12 predisposed patients.[1]

1. Rassmussen K, *et al*. Atrial fibrillation induced by atenolol. *Eur Heart J* 1982; **3:** 276–81.

Effects on lipid metabolism. For a report of acute pancreatitis due to hypertriglyceridaemia in a patient taking atenolol and metoprolol, see p.1227.

Effects on the liver. Adverse hepatic reactions in patients receiving atenolol have included reversible cholestatic hepatitis in one[1] and hepatic dysfunction in another.[2]

1. Schwartz MS, *et al.* Atenolol-associated cholestasis. *Am J Gastroenterol* 1989; **84:** 1084–6.
2. Yusuf SW, Mishra RM. Hepatic dysfunction associated with atenolol. *Lancet* 1995; **346:** 192.

Overdosage. Atenolol appears to lack membrane-stabilising activity and may have fewer adverse cardiac effects than some other beta blockers. However, cardiovascular toxicity has been noted after massive overdosage: ventricular asystole[1] and hypotension with ECG abnormalities[2] have been reported. Severe cardiovascular effects also occurred[3] in a patient with mixed overdosage including atenolol and diltiazem, and were attributed to additive toxicity.

1. Stinson J, *et al*. Ventricular asystole and overdose with atenolol. *BMJ* 1992; **305:** 693.
2. Love JN, Elshami J. Cardiovascular depression resulting from atenolol intoxication. *Eur J Emerg Med* 2002; **9:** 111–14.
3. Snook CP, *et al*. Severe atenolol and diltiazem overdose. *J Toxicol Clin Toxicol* 2000; **38:** 661–5.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Pharmacokinetics

About 50% of an oral dose of atenolol is absorbed. Peak plasma concentrations are reached in 2 to 4 hours. Atenolol has low lipid solubility. It crosses the placenta and is distributed into breast milk where concentrations higher than those in maternal plasma have been achieved. Only small amounts are reported to cross the blood-brain barrier, and plasma-protein binding is minimal. The plasma half-life is about 6 to 7 hours. Atenolol undergoes little or no hepatic metabolism and is excreted mainly in the urine. It is removed by haemodialysis.

Breast feeding. Atenolol diffuses into breast milk in concentrations similar[1] to or higher[2] than those in maternal blood. Cyanosis and bradycardia associated with ingestion of atenolol in breast milk has been reported in a 5-day-old term infant. The baby improved when breast feeding was stopped.[3]

1. Thorley KJ, McAinsh J. Levels of the beta-blockers atenolol and propranolol in the breast milk of women treated for hypertension in pregnancy. *Biopharm Drug Dispos* 1983; **4:** 299–301.
2. White WB, *et al*. Atenolol in human plasma and breast milk. *Obstet Gynecol* 1984; **63:** 42S–44S.
3. Schimmel MS, *et al*. Toxic effects of atenolol consumed during breast feeding. *J Pediatr* 1989; **114:** 476–8.

Pregnancy. Creatinine clearance increases during pregnancy, and a study in 17 pregnant patients found that the elimination half-life was shorter and renal clearance of atenolol faster during the second and third trimesters compared with three months post partum.[1] In another study,[2] postpartum samples were taken from the maternal and umbilical serum of 6 women who had been taking atenolol for at least 6 days before delivery; atenolol was detected in both maternal and cord blood in about equal concentrations. Atenolol was not detected in the maternal or cord blood of another patient who had stopped taking atenolol one day before delivery; the authors concluded that atenolol levels in the mother and fetus are equal at steady state, and that fetal accumulation does not occur. Atenolol concentrations in 35 term neonates whose mothers had received atenolol were examined.[3] It was found that the elimination rate for the neonates was 4 times slower than in adults, possibly because of immaturity of renal function. Transient bradycardia developed in 14 neonates.

1. Hebert MF, *et al*. Pharmacokinetics and pharmacodynamics of atenolol during pregnancy and postpartum. *J Clin Pharmacol* 2005; **45:** 25–33.
2. Melander A, *et al*. Transplacental passage of atenolol in man. *Eur J Clin Pharmacol* 1978; **14:** 93–4.
3. Rubin PC, *et al*. Atenolol elimination in the neonate. *Br J Clin Pharmacol* 1983; **16:** 659–62.

Uses and Administration

Atenolol is a cardioselective beta blocker (p.1225). It is reported to lack intrinsic sympathomimetic activity and membrane-stabilising properties.

Atenolol is used in the management of hypertension (p.1171), angina pectoris (p.1157), cardiac arrhythmias (p.1160), and myocardial infarction (p.1175). It may also be used for the prophylaxis of migraine (p.616).

In **hypertension** atenolol is given orally in a dose of 50 to 100 mg daily, as a single dose, although 50 mg daily is generally adequate. The full effect is usually evident within 1 to 2 weeks.

The usual dose for **angina pectoris** is 50 to 100 mg daily orally, given as a single dose or in divided doses. Additional benefit is not usually obtained from higher doses of atenolol although up to 200 mg daily has been given.

For the emergency treatment of **cardiac arrhythmias** atenolol may be given by intravenous injection in a dose of 2.5 mg injected at a rate of 1 mg/minute, repeated if necessary every 5 minutes to a maximum total dosage of 10 mg. Alternatively atenolol may be given by intravenous infusion over 20 minutes in a dose of 150 micrograms/kg. The injection or infusion procedure may be repeated every 12 hours if necessary. When control is achieved maintenance oral doses of 50 to 100 mg daily may be given.

Atenolol is also used in the early management of acute **myocardial infarction**. Treatment should be given within 12 hours of the onset of chest pain; atenolol 5 to 10 mg should be given by slow intravenous injection at a rate of 1 mg/minute, followed after 15 minutes with 50 mg orally, provided no adverse effects result from the injection; alternatively an intravenous dose of 5 mg may be repeated after 10 minutes followed by an oral dose of 50 mg after a further 10 minutes. A further 50 mg may be given orally after 12 hours, and subsequent dosage maintained, after a further 12 hours, with 100 mg daily.

In the prophylaxis of **migraine** an oral dose of 50 to 100 mg daily has been used.

Reduced doses may be required in patients with impaired renal function (see below).

Administration in renal impairment. The dose of atenolol should be reduced in patients with renal impairment, depending on the creatinine clearance (CC) as follows:

- CC 15 to 35 mL/minute per 1.73 m^2: 50 mg daily orally or 10 mg once every two days intravenously
- CC less than 15 mL/minute per 1.73 m^2: 25 mg daily or 50 mg on alternate days orally or 10 mg once every four days intravenously
- dialysis patients: 25 to 50 mg orally after each dialysis.

Preparations

BP 2008: Atenolol Injection; Atenolol Oral Solution; Atenolol Tablets; Cotenidone Tablets;
USP 31: Atenolol and Chlorthalidone Tablets; Atenolol Injection; Atenolol Oral Solution; Atenolol Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Atel; Atenoblock; Atenovit; Cardioblock; Corpaz; Fabotenol; Felobits; Ilaten; Myocord; Plenacor; Prenormine; Telvodin; Tensilol; Tozolden; Vericordin; ***Austral.:*** Anselol; Atehexal; Noten; Tenormin; Tensig; ***Austria:*** Arcablock; Atehexal; Atenolan; Atenotyrol†; Betasyn; Tenormin; ***Belg.:*** Atenotop; Athenol†; Docateno; Tenormin; ***Braz.:*** Ablok; Angipress; Atecard; Atenegran; Ateneo; Atenobal; Atenokin; Atenol; Atenolab; Atenopress†; Atenorm; Atenuol; Atepress; Biotenor†; Ditenol†; Neotenol†; Plenacor; Sifnolol†; ***Canad.:*** Apo-Atenol; Novo-Atenol; Nu-Atenol; Tenolin†; Tenormin; ***Chile:*** Betacar; Grifotenol; Labotensil; Tenormin†; ***Cz.:*** Apo-Atenol; Ateblocor†; Atehexal; Atenobene; Catenol†; Corotenol†; Tenormin; ***Denm.:*** Atenet; Atenodan; Atenor; Tenormin; Uniloc; ***Fin.:*** Atenblock; Atenol; Tenoblock; Tenoprin; ***Fr.:*** Betatop; Tenormine; ***Ger.:*** Ate Lich; Ate†; Atebeta; Atehexal; Atendol†; Ateno; Atenogamma; Blocotenol†; Cuxanorm; duratenol†; Evitocor†; Falitonsin†; Jenatenol; Juvental; Tenormin; ***Gr.:*** Adenamin; Azectol; Blocotenol; Estanolin†; Fealin; Galol†; Hemon†; Mesonex; Mezarid†; Neocardon; Silder†; Synarome; Tenormin; Tradiver†; Umoder; ***Hong Kong:*** Adoll; Antipressan; Apo-Atenol; Ateno†; CP-Atenol; Hypernol; Lo-Ten; Martenol; Normaten; Nortelol; Oraday; Tenormin; Ternolol; Tredol; Vascoten; Velorin; ***Hung.:*** Atenobene; Atenomel; Blokium; Huma-Atenol†; Prinorm; ***India:*** Atecard†; Aten; Beta; Beten; Cadpres; Hipres; Lonol; Teno; Tenolol; Tenormin; Tensimin†; ***Indon.:*** Betablok; Farnormin; Hiblok; Internolol; Tenblok; Tenormin; Tensinorm; Zumablok; ***Irl.:*** Amolin; Atecor; Ateni; Atenogen; Atenomel; Tenormin; Trantalol; ***Israel:*** Normalol; Normiten; ***Ital.:*** Atenol; Atermin; Seles Beta; Tenomax; Tenormin; ***Malaysia:*** Apo-Atenol; Beten; Corotenol†; Loten; Normaten†; Noten; Oraday†; Ranlol; Renotol†; Tenormin; Ternolol†; Uphanormin†; Urosin; Vascoten; ***Mex.:*** Atenol; Atoken; Biofilen; Blotex; Min-T; Nosbal; Tenormin; Trebanol; ***Neth.:*** Tenormin; ***Norw.:*** Alinor†; Tenormin; Uniloc; ***NZ:*** Anselol†; Lo-Ten; ***Philipp.:*** Atestad; Cardioten; Durabeta; Tenor-Bloc; Tenormin; Tenostat; Tensimin; Therabloc; Velorin; ***Pol.:*** Normocard; ***Port.:*** Ancoren†; Atenolac†; Blokium†; Tenormin; Tessifol; ***Rus.:*** Atenolan (Атенолан); Betacard (Бетакард); Catenol (Катенол); Hypoten (Хайпотен); Tenolol (Тенолол); ***S.Afr.:*** Atenoblok; B-Vasc†; Hexa-Blok; Ten-Bloka; Tenormin; Venapulse; ***Singapore:*** Alonet†; Apo-Atenol; Hypernol; Normaten; Noten; Prenolol; Tenolol; Tenormin; Ternolol†; Vascoten; Velorin†; ***Spain:*** Blokium; Neatenol; Tanser; Tenormin; ***Swed.:*** Selinol†; Tenormin; Uniloc†; ***Switz.:*** Atenil; ateno-basan†; Atesifar†; Cardaxen; Primatenol†; Selobloc; Tenormin; ***Thai.:*** Atcard; Atenol; Coratol; Nolol; Nortelol; Oraday; Preloc; Prenolol; Tenocor; Tenol; Tenolol; Tenormin; Tetalin; Vascoten; Velorin; ***Turk.:*** Nortan; Tensidif; Tensinor; ***UAE:*** Tensotin; ***UK:*** Antipressan; Atenix; Tenormin; ***USA:*** Tenormin; ***Venez.:*** Artenolol†; Atenoval†; Beloc; Blokium; Ritmilan; Tenormin.

Multi-ingredient: ***Arg.:*** Atel C†; Atel N†; Plenacor D; Prenomod†; Prenoretic; Vericordin Compuesto; ***Austria:*** Arcablock comp; Atenolan comp; Atenolol comp; Atenotyrol comp†; Beta-Adalat; Nif-Ten; Polinorm; Tenoretic; ***Belg.:*** Beta-Adalat†; Kalten†; Tenif; Tenoretic; ***Braz.:*** Ablok Plus; Angipress CD; Atenoclor†; Atenoric; Atenuol CRT; Betalor; Nifelat; Tenoretic; ***Canad.:*** Apo-Atenidone; Tenoretic; ***Chile:*** Tenoretic†; ***Cz.:*** Atedon†; Atenolol Compositum†; Tenoretic; ***Denm.:*** Tenidon; Tenoretic; ***Fin.:*** Nif-Ten; ***Fr.:*** Beta-Adalate; Tenordate; Tenoretic; ***Ger.:*** Ate Lich comp; Atehexal comp; Atel; AteNif beta; Ateno comp; Atenogamma comp; Atenolol AL comp; Atenolol comp; Blocotenol comp†; Bresben; Diu-Atenolol; duratenol comp†; Nif-Ten; Nifatenol; Sigabloc†; Teneretic; TRI-Normin; ***Gr.:*** Apress†; Chlotenor; Obosan; Tenoretic; Typofen; ***Hong Kong:*** Nif-Ten; Target; Tenoret; Tenoretic; ***Hung.:*** Atenolol Comp†; Blokium Diu; ***India:*** Amdepin-AT; Amlopres AT; Amlosafe-AT†; Amlostat-AT; Atecard-D†; Beta Nicardia†; Cardif Beta; Cardules Plus; Depten; Hipres-D; Lerez-AT†; Nifetolol; Presolar; Tenochek; Tenodor; Tenofed; Tenolol-AM; Tenolol-D†; Tenoric; ***Indon.:*** Nif-Ten; Tenoret; Tenoretic; ***Irl.:*** Atecor CT; Atenetic; Beta-Adalat; Nif-Ten; Tenoret; Tenoretic; ***Ital.:*** Atenigron; Atinorm; Carmian; Clortanol; Diube; Eupres; Igroseles; Mixer; Nif-Ten; Nor-Pa; Normopress; Target; Tenolone†; Tenoretic; ***Malaysia:*** Apo-Atenidone; Pretenol C; Target; Tenoret; Tenoretic; ***Mex.:*** Plenacor; Tenoretic; ***Neth.:*** Nif-Ten†; Tenoretic; ***Philipp.:*** Nif-Ten; Tenoretic; ***Port.:*** Blokium Diu†; Tenoretic; ***Rus.:*** Atehexal Compositum (Атегексал Композитум); Tenochek (Теночек); Tenoric (Тенорик); Tenorox (Тенорокс); ***S.Afr.:*** Adco-Loten; Atenoblok Co†; Tenchlor; Tenoretic; ***Singapore:*** Beta Nicardia; Nif-Ten; Nifetex; Tenoret; Tenoretic; ***Spain:*** Blokium Diu; Kalten; Neatenol Diu; Neatenol Diuvas; Normopresil; Tenoretic; ***Switz.:*** Atedurex; ateno-basan comp†; Beta-Adalat; Cardaxen plus; Co-Atenolol†; Cotenolol-Neo; Cotesifar†; Kalten; Nif-Atenil; Nif-Ten; Primatenol Plus†; Tenoretic; ***Thai.:*** Tenoret†; Tenoretic†; ***Turk.:*** Tenoretic; ***UK:*** AtenixCo; Beta-Adalat; Kalten; Tenchlor; Tenif; Tenoret; Tenoretic; Totaretic; ***USA:*** Tenoretic; ***Venez.:*** Blokturet; Tenoretic.

Atorvastatin Calcium *(BANM, USAN, rINNM)*

Atorvastatina cálcica; Atorvastatine calcique; Atorvastatinum calcicum; Calcii Atorvastatinum; CI-981. Calcium (β*R*,δ*R*)-2-(*p*-fluorophenyl)-β,δ-dihydroxy-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)pyrrole-1-heptanoic acid (1:2) trihydrate.

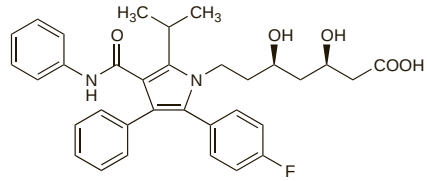
Кальций Аторвастатин

$C_{66}H_{68}CaF_2N_4O_{10}.3H_2O$ = 1209.4.

CAS — 134523-00-5 (atorvastatin); 134523-03-8 (atorvastatin calcium).

ATC — C10AA05.

ATC Vet — QC10AA05.



(atorvastatin)

Adverse Effects and Precautions

As for Simvastatin, p.1390.

◊ General references.

1. Black DM, *et al*. An overview of the clinical safety profile of atorvastatin (Lipitor), a new HMG-CoA reductase inhibitor. *Arch Intern Med* 1998; **158:** 577–84.
2. Bernini F, *et al*. Safety of HMG-CoA reductase inhibitors: focus on atorvastatin. *Cardiovasc Drugs Ther* 2001; **15:** 211–18.
3. Waters DD. Safety of high-dose atorvastatin therapy. *Am J Cardiol* 2005; **96** (suppl 5A): 69F–75F.
4. Arca M. Atorvastatin: a safety and tolerability profile. *Drugs* 2007; **67** (suppl 1): 63–9.

Effects on the skin. Toxic epidermal necrolysis apparently caused by atorvastatin has been reported.[1] The authors were not aware of this adverse effect previously having been associated with any of the statin lipid regulating drugs.

1. Pfeiffer CM, *et al*. Toxic epidermal necrolysis from atorvastatin. *JAMA* 1998; **279:** 1613–14.

Interactions

As for Simvastatin, p.1392.

Pharmacokinetics

Atorvastatin is rapidly absorbed from the gastrointestinal tract. It has low absolute bioavailability of about 12% due to presystemic clearance in the gastrointestinal mucosa and/or first-pass metabolism in the liver, its primary site of action. Atorvastatin is metabolised by the cytochrome P450 isoenzyme CYP3A4 to a number of active metabolites. It is 98% bound to plasma proteins. The mean plasma elimination half-life of atorvastatin is about 14 hours although the half-life of inhibitory activity for HMG-CoA reductase is about 20 to 30 hours due to the contribution of the active metabolites. Atorvastatin is excreted as metabolites, primarily in the bile.

◊ Reviews.

1. Lennernäs H. Clinical pharmacokinetics of atorvastatin. *Clin Pharmacokinet* 2003; **42:** 1141–60.

Uses and Administration

Atorvastatin, a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (or statin), is a lipid regulating drug with actions on plasma lipids similar to those of simvastatin (p.1394). It is used to reduce LDL-cholesterol, apolipoprotein B, and triglycerides, and to increase HDL-cholesterol in the treatment of hyperlipidaemias (p.1169), including hypercholesterolaemias and combined (mixed) hyperlipidaemia (type IIa or IIb hyperlipoproteinaemias), hypertriglyceridaemia (type IV), and dysbetalipoproteinaemia (type III). Atorvastatin can be effective as adjunctive therapy in patients with homozygous familial hypercholesterolaemia who have some LDL-receptor function. It is also used for primary and secondary prophylaxis of cardiovascular events (see Cardiovascular Risk Reduction, p.1164) in patients with multiple risk factors, including diabetes mellitus.

Atorvastatin is given orally as the calcium salt although doses are expressed in terms of the base; 10.82 mg of atorvastatin calcium trihydrate is equivalent to 10 mg of base. The usual initial dose is 10 to 20 mg of atorvastatin once daily; an initial dose of 40 mg daily may be used in patients who require a large reduction in LDL-cholesterol. The dose may be adjusted at intervals of 4 weeks up to a maximum of 80 mg daily.

For patients taking drugs that interact with atorvastatin, dose reduction is advised as follows:

- patients taking *ciclosporin*, maximum dose 10 mg once daily
- patients taking *clarithromycin*, initial dose 10 mg once daily and maximum dose 20 mg once daily
- patients taking *itraconazole*, initial dose 10 mg once daily and maximum dose 40 mg once daily
- patients taking *ritonavir-boosted lopinavir* or *ritonavir-boosted saquinavir*, doses above 20 mg once daily should be used with caution

For the use of atorvastatin in children and adolescents, see below.

◊ General reviews.

1. Lea AP, McTavish D. Atorvastatin: a review of its pharmacology and therapeutic potential in the management of hyperlipidaemias. *Drugs* 1997; **53:** 828–47.
2. Malinowski JM. Atorvastatin: a hydroxymethylglutaryl-coenzyme A reductase inhibitor. *Am J Health-Syst Pharm* 1998; **55:** 2253–67.
3. Malhotra HS, Goa KL. Atorvastatin: an updated review of its pharmacological properties and use in dyslipidaemia. *Drugs* 2001; **61:** 1835–81.
4. Croom KF, Plosker GL. Atorvastatin: a review of its use in the primary prevention of cardiovascular events in patients with type 2 diabetes mellitus. *Drugs* 2005; **65:** 137–52.
5. Poli A. Atorvastatin: pharmacological characteristics and lipid-lowering effects. *Drugs* 2007; **67** (suppl 1): 3–15.
6. Bybee KA, *et al.* Cumulative clinical trial data on atorvastatin for reducing cardiovascular events: the clinical impact of atorvastatin. *Curr Med Res Opin* 2008; **24:** 1217–29.

Administration in children. In children and adolescents aged 10 to 17 years with hypercholesterolaemia or combined (mixed) hyperlipidaemia, atorvastatin is licensed for use orally in an initial dose of 10 mg once daily, adjusted if necessary at intervals of at least 4 weeks to a maximum dose of 20 mg once daily. A 6-month study[1] with this dose regimen in children with familial or severe hypercholesterolaemia found that atorvastatin was both safe and effective. Atorvastatin has also been used in children with hyperlipidaemia associated with renal[2] or heart[3] transplantation.

1. McCrindle BW, *et al.* Efficacy and safety of atorvastatin in children and adolescents with familial hypercholesterolemia or severe hyperlipidemia: a multicenter, randomized, placebo-controlled trial. *J Pediatr* 2003; **143:** 74–80.
2. Argent E, *et al.* Atorvastatin treatment for hyperlipidemia in pediatric renal transplant recipients. *Pediatr Transplant* 2003; **7:** 38–42.
3. Chin C, *et al.* Efficacy and safety of atorvastatin after pediatric heart transplantation. *J Heart Lung Transplant* 2002; **21:** 1213–17.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ampliar; Atarva; Ateroclar; Atorvastan; Finlipol; Liparex; Lipibec; Lipifen; Lipitor; Lipocambi; Lipofin; Liponorm; Lipostop; Lipovastinklonal; Normalip; Plan; Tialipol; Torivas; Vastina; Zarator; ***Austral.:*** Lipitor; ***Austria:*** Sortis; ***Belg.:*** Lipitor; ***Braz.:*** Citalor; Lipitor; ***Canad.:*** Lipitor; ***Chile:*** Atenfar; Atorlip; Dislipor; Hipolixan; Lipitor; Lipotropic; Lipox; Lowden; Zarator; Zurinel; ***Cz.:*** Atogal; Atoris; Atorpharm; Bisatum; Sortis; Torvacard; Triglyx; Tulip; Vaston; ***Denm.:*** Zarator; ***Fin.:*** Lipitor; ***Fr.:*** Tahor; ***Ger.:*** Sortis; ***Gr.:*** Altoram; Antorcin; Arvastatil; Ator-Chol; Atorgon; Atorolnga; Atorstat; Atorval; Atorvanox; Atorvin; Atrost; Atrosterol; Atrovita; Biger; Delipost; Holisten; Lipigan; Lipitor; Lipizem; Lipodial; Lipostatin; Lipovast; Lorvaten; Rotova; Torvastin; Vastazor; Xanator; Zarator; ***Hong Kong:*** Lipitor; ***Hung.:*** Atoris; Atorva; Atorvox; Hypolip; Liprimar; Sortis; Torvacard; ***India:*** Atorlip; Atorva; Attor; Liporest; X'tor; ***Indon.:*** Atorsan; Lipitor; ***Irl.:*** Lipitor; ***Israel:*** Lipitor; Torid; ***Ital.:*** Lipitor†; Torvast; Totalip; Xarator†; ***Jpn:*** Lipitor; ***Malaysia:*** Lipitor; Storvas; ***Mex.:*** Lipitor; ***Neth.:*** Cardyl; Lipitor; Prevencor; Zarator; ***Norw.:*** Lipitor; ***NZ:*** Lipitor; ***Philipp.:*** Lipitor; ***Pol.:*** Atoris; Atrox; Sortis; Torvacard; Tulip; ***Port.:*** Sortis; Zarator; ***Rus.:*** Atomax (Атомакс); Atoris (Аторис); Liprimar (Липримар); Liptonorm (Липтонорм); Torvacard (Торвакард); Tulip (Тулип); ***S.Afr.:*** Lipitor; ***Singapore:*** Lipitor; ***Spain:*** Cardyl; Prevencor; Zarator; ***Swed.:*** Lipitor; ***Switz.:*** Sortis; ***Thai.:*** Lipitor; ***Turk.:*** Ator; Kolestor; Lipitaksin; Lipitor; Saphire; Tarden; ***UK:*** Lipitor; ***USA:*** CTR; Lipitor; ***Venez.:*** Atovarol; Glustar; Lipitor; Tarimyl.

Multi-ingredient: ***Arg.:*** Ampliar Duo; Ateroclar Duo; Hipertensal Combi; Liparex Duo; Lipibec Duo; Lipoarteriosan; Liponorm Duo; Torimibe; ***Austral.:*** Caduet; ***Braz.:*** Caduet; ***Chile:*** Caduet; ***Cz.:*** Caduet; ***Fr.:*** Caduet; ***Hung.:*** Caduet; ***India:*** Zetitor†; ***Malaysia:*** Caduet; ***Mex.:*** Caduet; ***Philipp.:*** Envacar; ***Port.:*** Caduet; ***S.Afr.:*** Caduet; ***Singapore:*** Caduet; ***USA:*** Caduet; ***Venez.:*** Caduet.

Atropine *(BAN)*

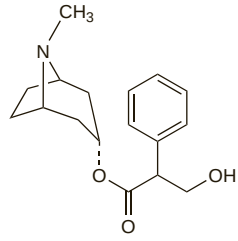
Atropiini; Atropin; Atropina; Atropinas; Atropinum; (±)-Hyoscyamine. (1*R*,3*r*,5*S*,8*r*)-Tropan-3-yl (*RS*)-tropate.

$C_{17}H_{23}NO_3$ = 289.4.

CAS — 51-55-8.

ATC — A03BA01; S01FA01.

ATC Vet — QA03BA01; QS01FA01.



Description. Atropine is an alkaloid that may be obtained from solanaceous plants, or prepared by synthesis.

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

Ph. Eur. 6.2 (Atropine). A white or almost white, crystalline powder or colourless crystals. Very slightly soluble in water; freely soluble in alcohol and in dichloromethane. Protect from light.

USP 31 (Atropine). White crystals, usually needle-like, or white crystalline powder. Soluble 1 in 460 of water, 1 in 90 of water at 80°, 1 in 2 of alcohol, 1 in 1 of chloroform, and 1 in 25 of ether; soluble in glycerol. Its saturated solution in water is alkaline to phenolphthalein. Store in airtight containers. Protect from light.

Atropine Methobromide *(BANM)*

Atropina, metilbromuro de; Atropine Methylbromide; Methylatropine Bromide; Méthylatropine, bromure de; Methylatropini bromidum; Methylatropinii Bromidum; Methylatropinium Bromatum; Methylatropinium-bromid; Metilatropin-bromid; Metilatropino bromidas; Metylatropinbromid; Metyyliatropiinibromidi; Mydriasine. (1*R*,3*r*,5*S*)-8-Methyl-3-[(±)-tropoyloxy]tropanium bromide.

$C_{18}H_{26}BrNO_3$ = 384.3.

CAS — 2870-71-5.

ATC — A03BA01.

ATC Vet — QA03BA01.

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

Ph. Eur. 6.2 (Methylatropine Bromide; Atropine Methobromide BP 2008). Colourless crystals or a white or almost white crystalline powder. Freely soluble in water; sparingly soluble in alcohol. Protect from light.

Atropine Methonitrate *(BANM, rINN)*

Atrop. Methonit.; Atropiinimetonitraatti; Atropine, Méthonitrate d'; Atropini Methonitras; Atropinmetonitrat; Methylatropine Nitrate *(USAN)*; Méthylatropine, nitrate de; Methylatropini nitras; Methylatropinii Nitras; Methylatropinium nitrát; Metilatropin-nitrát; Metilatropino nitratas; Metilnitrato de atropina; Metonitrato de atropina; Metylatropinnitrat; Metyyliatropiininitraatti. (1*R*,3*r*,5*S*)-8-Methyl-3-[(±)-tropoyloxy]tropanium nitrate.

Атропина Метонитрат

$C_{18}H_{26}N_2O_6$ = 366.4.

CAS — 52-88-0.

ATC — A03BB02.

ATC Vet — QA03BB02.

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

Ph. Eur. 6.2 (Methylatropine Nitrate; Atropine Methonitrate BP 2008). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; soluble in alcohol. Protect from light.

Stability. Aqueous solutions of atropine methonitrate are unstable; stability is enhanced in acid solutions of pH below 6.

Atropine Sulfate

Atrop. Sulph.; Atropiinisulfaatti; Atropin Sülfat; Atropina, sulfato de; Atropine, sulfate d'; Atropine Sulphate *(BANM)*; Atropini sulfas; Atropini Sulfas Monohydricus; Atropino sulfatas; Atropinsulfat; Atropin-sulfát monohydrát; Atropin-szulfát; Atropiny siarczan.

$(C_{17}H_{23}NO_3)_2,H_2SO_4,H_2O$ = 694.8.

CAS — 55-48-1 (anhydrous atropine sulfate); 5908-99-6 (atropine sulfate monohydrate).

ATC — A03BA01; S01FA01.

ATC Vet — QA03BA01; QS01FA01.

NOTE. Compounded preparations of atropine sulfate may be represented by the following names:

- Co-phenotrope (*BAN*)—atropine sulfate 1 part and diphenoxylate hydrochloride 100 parts (w/w).
  ATR is a code approved by the BP 2008 for use on single unit dose eye drops containing atropine sulfate 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.*

Ph. Eur. 6.2 (Atropine Sulphate). A white or almost white, crystalline powder or colourless crystals. Very soluble in water; freely soluble in alcohol. A 2% solution in water has a pH of 4.5 to 6.2. Protect from light.

USP 31 (Atropine Sulfate). Odourless, colourless crystals or white crystalline powder. It effloresces in dry air. Soluble 1 in 0.5 of water, 1 in 2.5 of boiling water, 1 in 5 of alcohol, and 1 in 2.5 of glycerol. Store in airtight containers.

Incompatibility. Incompatibility between atropine sulfate and hydroxybenzoate preservatives has been seen,[1] resulting in a total loss of the atropine in 2 to 3 weeks.

1. Deeks T. Oral atropine sulphate mixtures. *Pharm J* 1983; **230:** 481.

Adverse Effects

The pattern of adverse effects seen with atropine and other antimuscarinics can mostly be related to their pharmacological actions at muscarinic and, at high doses, nicotinic receptors (see Actions of Antimuscarinics, below). These effects are dose-related and are usually reversible when therapy is stopped. The **peripheral** effects of atropine and other antimuscarinics are a consequence of their inhibitory effect on muscarinic receptors within the autonomic nervous system. At therapeutic doses, adverse effects include dryness of the mouth with difficulty in swallowing and talking, thirst, reduced bronchial secretions, dilatation of the pupils (mydriasis) with loss of accommodation (cycloplegia) and photophobia, flushing and dryness of the skin, transient bradycardia followed by tachycardia, with palpitations and arrhythmias, and difficulty in micturition, as well as reduction in the tone and motility of the gastrointestinal tract leading to constipation. Some of the **central** effects of atropine and other tertiary antimuscarinics seen at toxic doses (see below) may also occur at therapeutic doses.

In **overdosage**, the peripheral effects become more pronounced and other symptoms such as hyperthermia, hypertension, increased respiratory rate, and nausea and vomiting may occur. A rash may appear on the face or upper trunk. Toxic doses also cause CNS stimulation marked by restlessness, confusion, excitement, ataxia, incoordination, paranoid and psychotic reac-