Argatroban *(BAN, USAN, rINN)*

Argatrobanum; Argipidine; DK-7419; GN-1600; MCI-9038; MD-805. (2*R*,4*R*)-4-Methyl-1-[(*S*)-N^2-{[(*RS*)-1,2,3,4-tetrahydro-3-methyl-8-quinolyl]sulfonyl}arginyl]pipecolic acid.

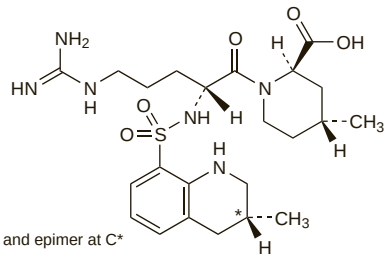
Аргатробан

$C_{23}H_{36}N_6O_5S$ = 508.6.

CAS — 74863-84-6 (anhydrous argatroban); 141396-28-3 (argatroban monohydrate).

ATC — B01AE03.

ATC Vet — QB01AE03.



Incompatibility. Trace evidence of precipitation was seen immediately after mixing solutions of argatroban and amiodarone.[1] No visual incompatibility was noted for solutions of argatroban with furosemide, nesiritide, sodium nitroprusside, or a total parenteral nutrition solution, but changes in pH occurred over 24 hours, suggesting such mixtures should be used with caution.[1]

1. Honisko ME, *et al.* Compatibility of argatroban with selected cardiovascular agents. *Am J Health-Syst Pharm* 2004; **61:** 2415–18.

Adverse Effects and Precautions

As for Lepirudin, p.1323.

If argatroban and warfarin are given together there is an effect on the measurement of the INR values. The manufacturer provides guidelines for interpreting the INR during the change from combined therapy to warfarin alone.

Administration in the critically ill. Four critically ill patients became excessively anticoagulated[1] when treatment with argatroban was started after cardiac surgery, despite use of only the recommended doses or lower. All four had relatively normal hepatic function. Clearance of the drug appeared to be prolonged after it was stopped. In a patient[2] who had no significant direct hepatic dysfunction but severe hepatic congestion secondary to acute renal failure, the effect of argatroban was prolonged and reduction in dose was necessary. Haemodialysis had little or no effect on clearance. Further cases of excessive anticoagulation have been reported in patients with multiple organ failure,[3] and in an elderly patient with multiple comorbidities.[4] Patients developing heparin-induced thrombocytopenia after cardiac surgery may also be more sensitive to argatroban, and an initial dose of 500 nanograms/kg per minute has been suggested.[5]

1. Reichert MG, *et al.* Excessive argatroban anticoagulation for heparin-induced thrombocytopenia. *Ann Pharmacother* 2003; **37:** 652–4.
2. de Denus S, Spinler SA. Decreased argatroban clearance unaffected by hemodialysis in anasarca. *Ann Pharmacother* 2003; **37:** 1237–40.
3. Beiderlinden M, *et al.* Argatroban anticoagulation in critically ill patients. *Ann Pharmacother* 2007; **41:** 749–54.
4. Kubiak DW, *et al.* Extensive prolongation of aPTT with argatroban in an elderly patient with improving renal function, normal hepatic enzymes, and metastatic lung cancer. *Ann Pharmacother* 2005; **39:** 1119–23.
5. Hoffman WD, *et al.* Reduced argatroban doses after coronary artery bypass graft surgery. *Ann Pharmacother* 2008; **42:** 309–16.

Overdosage. A critically ill patient receiving low-dose continuous intravenous argatroban for thromboembolism prophylaxis was mistakenly given an additional infusion of 125 mg of argatroban over 1 hour (26.1 micrograms/kg per minute).[1] He was given repeated doses of fresh frozen plasma and no bleeding complications occurred, but the prothrombin time remained prolonged for over 48 hours. Although the total dose given was comparable to doses used in other indications, critically ill patients may be particularly sensitive to the effects of argatroban (see above).

1. Yee AJ, Kuter DJ. Successful recovery after an overdose of argatroban. *Ann Pharmacother* 2006; **40:** 336–9.

Interactions

As for Lepirudin, p.1323.

Warfarin. Although caution is necessary in interpreting the INR when argatroban and warfarin are given together (see Adverse Effects and Precautions, above), a study in healthy subjects[1] showed no pharmacokinetic interaction.

1. Brown PM, Hursting MJ. Lack of pharmacokinetic interactions between argatroban and warfarin. *Am J Health-Syst Pharm* 2002; **59:** 2078–83.

Pharmacokinetics

Argatroban is about 54% bound to plasma proteins. Metabolism, mainly hydroxylation and aromatisation, takes place in the liver, with the main metabolite having weak anticoagulant activity. Anticoagulant effects are seen immediately upon starting infusion; steady-state concentrations occur within 1 to 3 hours and are maintained until the infusion is stopped or the dose adjusted. The terminal elimination half-life of argatroban is between 39 and 51 minutes. It is excreted primarily in the faeces, via the bile as metabolites and as unchanged drug. About 16% of a dose is excreted unchanged in the urine, and at least 14% unchanged in faeces.

Uses and Administration

Argatroban is a synthetic direct thrombin inhibitor (see Lepirudin, p.1323) with anticoagulant and antiplatelet activity. It is used for the treatment and prophylaxis of thromboembolism in patients with heparin-induced thrombocytopenia (see Effects on the Blood under Heparin, p.1302), and as an adjunct in patients undergoing percutaneous coronary interventions (see Reperfusion and Revascularisation Procedures, p.1181) who have or are at risk of heparin-induced thrombocytopenia. It has also been used in other thromboembolic disorders.

In the management of heparin-induced thrombocytopenia, argatroban is given by intravenous infusion in an initial dose of 2 micrograms/kg per minute, adjusted according to the activated partial thromboplastin time (APTT), to a maximum dose of 10 micrograms/kg per minute.

In percutaneous coronary interventions in patients at risk of or with heparin-induced thrombocytopenia, argatroban is given by intravenous infusion in an initial dose of 25 micrograms/kg per minute, and an intravenous injection of 350 micrograms/kg is given simultaneously over 3 to 5 minutes. Close monitoring of the activated clotting time (ACT) is required. If necessary, additional intravenous bolus doses of 150 micrograms/kg may be given, and the infusion rate adjusted to between 15 and 40 micrograms/kg per minute.

Doses should be reduced in patients with hepatic impairment (see below).

◊ References.

1. Kondo LM, *et al.* Argatroban for prevention and treatment of thromboembolism in heparin-induced thrombocytopenia. *Ann Pharmacother* 2001; **35:** 440–51.
2. McKeage K, Plosker GL. Argatroban. *Drugs* 2001; **61:** 515–22.
3. Verme-Gibboney CN, Hursting MJ. Argatroban dosing in patients with heparin-induced thrombocytopenia. *Ann Pharmacother* 2003; **37:** 970–5.
4. Lewis BE, *et al.* Effects of argatroban therapy, demographic variables, and platelet count on thrombotic risks in heparin-induced thrombocytopenia. *Chest* 2006; **129:** 1407–16.
5. Martin ME, *et al.* Argatroban for anticoagulation during cardiac surgery. *Eur J Haematol* 2007; **78:** 161–6.
6. Bartholomew JR, *et al.* Argatroban anticoagulation for heparin-induced thrombocytopenia in elderly patients. *Drugs Aging* 2007; **24:** 489–99.
7. Beiderlinden M, *et al.* Argatroban in extracorporeal membrane oxygenation. *Artif Organs* 2007; **31:** 461–5.
8. Boggio LN, Oza VM. Argatroban use in heparin-induced thrombocytopenia. *Expert Opin Pharmacother* 2008; **9:** 1963–7.

Administration in hepatic impairment. In patients with heparin-induced thrombocytopenia with hepatic impairment the initial dose of argatroban should be reduced.[1] US licensed product information recommends an initial dose of 500 nanograms/kg per minute in moderate hepatic impairment. Reversal of anticoagulant effects after stopping argatroban may take more than 4 hours, due to decreased clearance and increased elimination half-life. High doses of argatroban should not be used in patients with significant hepatic impairment undergoing percutaneous coronary interventions.

1. Levine RL, *et al.* Argatroban therapy in heparin-induced thrombocytopenia with hepatic dysfunction. *Chest* 2006; **129:** 1167–75.

Administration in renal impairment. Argatroban is not significantly excreted by the kidneys and dosage adjustment is not usually required in renal impairment, although excessive anticoagulation has been reported in critically ill patients, including some with compromised renal function (see Administration in the Critically Ill under Adverse Effects, above). Argatroban has been successfully used for anticoagulation in patients undergoing chronic haemodialysis who developed thrombocytopenia with heparin.[1] Argatroban was not significantly removed by dialysis and no dosage adjustment was required. The use of argatroban in patients with renal impairment has been reviewed.[2]

1. Tang IY, *et al.* Argatroban and renal replacement therapy in patients with heparin-induced thrombocytopenia. *Ann Pharmacother* 2005; **39:** 231–6.
2. Hursting MJ, Murray PT. Argatroban anticoagulation in renal dysfunction: a literature analysis. *Nephron Clin Pract* 2008; **109:** c80–c94.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Novastan; ***Neth.:*** Arganova; ***Swed.:*** Novastan; ***USA:*** Argatroban.

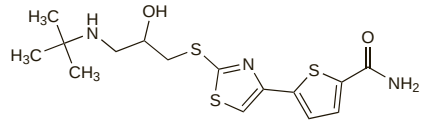
Arotinolol Hydrochloride *(rINNM)* ⊗

Arotinolol, Chlorhydrate d'; Arotinololi Hydrochloridum; Hidrocloruro de arotinolol; S-596. (±)-5-[2-{[3-(*tert*-Butylamino)-2-hydroxypropyl]thio}-4-thiazolyl]-2-thiophenecarboxamide hydrochloride.

Аротинолола Гидрохлорид

$C_{15}H_{21}N_3O_2S_3$,HCl = 408.0.

CAS — 68377-92-4 (arotinolol); 68377-91-3 (arotinolol hydrochloride).



(arotinolol)

Pharmacopoeias. In *Jpn.*

Profile

Arotinolol is a non-cardioselective beta blocker (p.1225); it also has $alpha_1$-blocking activity. It is used as the hydrochloride in the management of hypertension (p.1171), angina pectoris (p.1157), cardiac arrhythmias (p.1160), and essential tremor (p.1231). The usual oral dose is 20 mg daily in 2 divided doses although up to 30 mg daily may be given. The initial dose for essential tremor is 10 mg daily.

Preparations

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

Atenolol *(BAN, USAN, rINN)* ⊗

Aténolol; Atenololi; Atenololis; Atenololum; ICI-66082. 2-{*p*-[2-Hydroxy-3-(isopropylamino)propoxy]phenyl}acetamide.

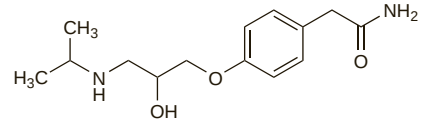
Атенолол

$C_{14}H_{22}N_2O_3$ = 266.3.

CAS — 29122-68-7; 60966-51-0.

ATC — C07AB03.

ATC Vet — QC07AB03.



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

- Co-tenidone (*BAN*)—atenolol 4 parts and chlortalidone 1 part (w/w)
- Co-tenidone (*PEN*)—atenolol and chlortalidone.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Atenolol). A white or almost white powder. Sparingly soluble in water; soluble in dehydrated alcohol; slightly soluble in dichloromethane.
USP 31 (Atenolol). White or practically white, odourless powder. Slightly soluble in water and in isopropyl alcohol; sparingly soluble in alcohol; freely soluble in methyl alcohol.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

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.:*** Blokiuret; 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.

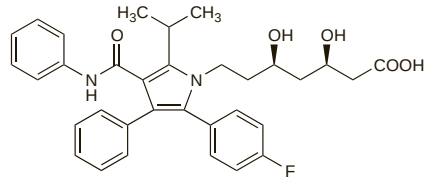
Кальций Аторвастатин

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