2. Reid JL. Rilmenidine: a clinical overview. *Am J Hypertens* 2000; **13:** 106S–111S.
3. Reid JL. Update on rilmenidine: clinical benefits. *Am J Hypertens* 2001; **14:** 322S–324S.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Hyperium; ***Austria:*** Iterium; ***Braz.:*** Hyperium; ***Cz.:*** Albarel; Tenaxum; ***Fr.:*** Hyperium; ***Hong Kong:*** Iperdix; ***Hung.:*** Hyperlex; Tenaxum; ***Philipp.:*** Hyperdix; ***Pol.:*** Tenaxum; ***Port.:*** Hyperium; ***Rus.:*** Albarel (Альбарел); ***Thai.:*** Hyperdix; ***Turk.:*** Hyperium; ***Venez.:*** Hyperium.

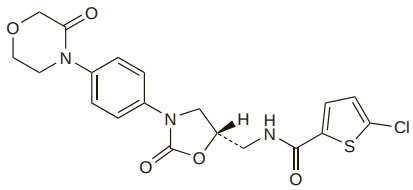
Rivaroxaban *(USAN, rINN)*

Bay-59-7939; Rivaroxabán; Rivaroxabanum. 5-Chloro-*N*-({(5*S*)-2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]-1,3-oxazolidin-5-yl}methyl)thiophene-2-carboxamide.

Ривароксабан

$C_{19}H_{18}ClN_3O_5S$ = 435.9.

CAS — 366789-02-8.



Profile

Rivaroxaban is an oral direct inhibitor of activated factor X that is under investigation in thromboembolic disorders.

◊ References.

1. Fisher WD, *et al.* Rivaroxaban for thromboprophylaxis after orthopaedic surgery: pooled analysis of two studies. *Thromb Haemost* 2007; **97:** 931–7.
2. Agnelli G, *et al.* Treatment of proximal deep-vein thrombosis with the oral direct factor Xa inhibitor rivaroxaban (BAY 59-7939): the ODIXa-DVT (Oral Direct Factor Xa Inhibitor BAY 59-7939 in Patients with Acute Symptomatic Deep-Vein Thrombosis) study. *Circulation* 2007; **116:** 180–7.
3. Eriksson BI, *et al.* RECORD1 Study Group. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med* 2008; **358:** 2765–75.
4. Lassen MR, *et al.* RECORD3 Investigators. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *N Engl J Med* 2008; **358:** 2776–86.
5. Kakkar AK, *et al.* RECORD2 Investigators. Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. *Lancet* 2008; **372:** 31–9.
6. Piccini JP, *et al.* Rivaroxaban, an oral direct factor Xa inhibitor. *Expert Opin Invest Drugs* 2008; **17:** 925–37.

Rosuvastatin Calcium *(BANM, USAN, rINNM)*

Calcii Rosuvastatinum; Rosuvastatina calcica; Rosuvastatine Calcique; S-4522; ZD-4522 (rosuvastatin). (*E*)-(3*R*,5*S*)-7-{4-(4-Fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl}-3,5-dihydroxyhept-6-enoic acid calcium (2:1).

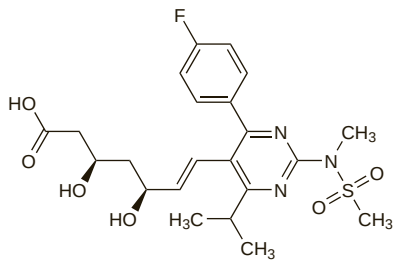
Кальций Розувастатин

$(C_{22}H_{27}FN_3O_6S)_2Ca$ = 1001.1.

CAS — 287714-41-4 (rosuvastatin); 147098-20-2 (rosuvastatin calcium).

ATC — C10AA07.

ATC Vet — QC10AA07.



(rosuvastatin)

Adverse Effects and Precautions

As for Simvastatin, p.1390. Systemic exposure to rosuvastatin may be higher in Asian patients (see Ethnicity under Pharmacokinetics, below) and lower doses are advised in Asians and in other patients at high risk of myopathy (see Uses and Administration, below).

Incidence of adverse effects. An analysis[1] of adverse effects reported to the FDA in the first year of marketing found that rosuvastatin was significantly more likely to be associated with severe adverse effects than some other statins. However, further analyses of data from clinical studies[2] and post-marketing studies[3,4] suggest that the risk of adverse effects is similar for all the statins. Another observational study[5] with a median treatment period of 9.8 months found that rosuvastatin was generally well tolerated, although 17.5% of patients stopped taking the drug, with myalgia being the most common reason. Abnormal liver function tests were more common in patients taking higher doses.

1. Alsheikh-Ali AA, *et al.* The safety of rosuvastatin as used in common clinical practice: a postmarketing analysis. *Circulation* 2005; **111:** 3051–7.
2. Shepherd J, *et al.* Safety of rosuvastatin: update on 16,876 rosuvastatin-treated patients in a multinational clinical trial program. *Cardiology* 2007; **107:** 433–43.
3. Goettsch WG, *et al.* Results from a rosuvastatin historical cohort study in more than 45 000 Dutch statin users, a PHARMO study. *Pharmacoepidemiol Drug Saf* 2006; **15:** 435–43.
4. McAfee AT, *et al.* The comparative safety of rosuvastatin: a retrospective matched cohort study in over 48 000 initiators of statin therapy. *Pharmacoepidemiol Drug Saf* 2006; **15:** 444–53.
5. Kasliwal R, *et al.* Safety profile of rosuvastatin: results of a prescription-event monitoring study of 11 680 patients. *Drug Safety* 2007; **30:** 157–70.

Interactions

The interactions of statins with other drugs are described under simvastatin, p.1392. Rosuvastatin undergoes limited metabolism, principally by the cytochrome P450 isoenzyme CYP2C9, and may not have the same interactions with enzyme inhibitors as simvastatin. However, increased plasma-rosuvastatin concentrations have been reported with ciclosporin, HIV-protease inhibitors, and, to a lesser extent, with gemfibrozil, and such combinations should be avoided. If they must be given together, lower doses of rosuvastatin should be used (see Uses and Administration, below); in UK licensed product information, rosuvastatin is contra-indicated with ciclosporin.

Pharmacokinetics

Rosuvastatin is incompletely absorbed from the gastrointestinal tract, with an absolute bioavailability of about 20%. Peak plasma concentrations are achieved about 5 hours after an oral dose. It is taken up extensively by the liver, its primary site of action, and undergoes limited metabolism, mainly by the cytochrome P450 isoenzyme CYP2C9. It is about 90% bound to plasma proteins. The plasma elimination half-life of rosuvastatin is about 19 hours. About 90% of an oral dose of rosuvastatin appears in the faeces, including absorbed and non-absorbed drug, and the remainder is excreted in the urine; about 5% of a dose is excreted unchanged in urine.

Ethnicity. A pharmacokinetic study[1] found that plasma exposure to rosuvastatin and its metabolites was significantly higher in Asian (Chinese, Malay, or Indian) than in Caucasian subjects and lower doses should be used (see Uses and Administration, below).

1. Lee E, *et al.* Rosuvastatin pharmacokinetics and pharmacogenetics in white and Asian subjects residing in the same environment. *Clin Pharmacol Ther* 2005; **78:** 330–41.

Uses and Administration

Rosuvastatin, a hydroxymethylglutaryl 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 management of hyperlipidaemias (p.1169), including primary hypercholesterolaemia (type IIa), mixed dyslipidaemia (type IIb), and hypertriglyceridaemia (type IV), as well as in patients with homozygous familial hypercholesterolaemia. It is also used to reduce the progression of atherosclerosis.

Rosuvastatin is given orally as the calcium salt, although doses are expressed in terms of the base; 10.4 mg of rosuvastatin calcium is equivalent to about 10 mg of base.

The usual initial dose of rosuvastatin is 5 or 10 mg once daily, depending on plasma-cholesterol concentrations, cardiovascular risk factors, and risk factors for adverse effects. The maintenance dose ranges from 5 to 40 mg once daily, although the 40-mg dose is reserved for patients with high cardiovascular risk who do not achieve their target cholesterol concentration at lower doses and who do not have risk factors for adverse effects. Specific dosage recommendations vary; for dosage in renal impairment, see below.

UK licensed product information recommends an initial dose of 5 or 10 mg once daily; elderly patients, Asians, and those at risk of myopathy should be given the 5-mg dose. The dose may be increased at intervals of 4 weeks, if necessary, to a usual maximum of 20 mg once daily. A higher dose of 40 mg once daily may be given under specialist supervision in severe hypercholesterolaemia, but should not be given to patients at high risk of myopathy, including those receiving fibrates, and Asian patients; use with *ciclosporin* is contra-indicated.

US licensed product information recommends a usual initial dose of 10 mg once daily. However, a lower initial dose of 5 mg once daily may be adequate and is recommended for patients at risk of myopathy, including Asian patients; patients with marked hypercholesterolaemia, such as those with homozygous familial hypercholesterolaemia, may be started on 20 mg once daily. The dose should be adjusted after 2 to 4 weeks, to a usual maximum of 20 mg once daily; a dose of 40 mg once daily may be necessary in some patients. Patients receiving *ciclosporin* may be given a maximum of 5 mg once daily, and in those receiving *gemfibrozil* or *ritonavir-boosted lopinavir* the maximum dose is 10 mg once daily; dosage increases should be made with caution in Asian patients.

◊ General reviews.

1. Chong PH, Yim BT. Rosuvastatin for the treatment of patients with hypercholesterolemia. *Ann Pharmacother* 2002; **36:** 93–101.
2. Carswell CI, *et al.* Rosuvastatin. *Drugs* 2002; **62:** 2075–85.
3. White CM. A review of the pharmacologic and pharmacokinetic aspects of rosuvastatin. *J Clin Pharmacol* 2002; **42:** 963–70.
4. McKenney JM. Efficacy and safety of rosuvastatin in treatment of dyslipidemia. *Am J Health-Syst Pharm* 2005; **62:**1033–47.
5. Olsson AG. Expanding options with a wider range of rosuvastatin doses. *Clin Ther* 2006; **28:** 1747–63.
6. Kapur NK. Rosuvastatin: a highly potent statin for the prevention and management of coronary artery disease. *Expert Rev Cardiovasc Ther* 2007; **5:** 161–75.
7. Schuster H. The GALAXY Program: an update on studies investigating efficacy and tolerability of rosuvastatin for reducing cardiovascular risk. *Expert Rev Cardiovasc Ther* 2007; **5:** 177–93.
8. Crouse JR. An evaluation of rosuvastatin: pharmacokinetics, clinical efficacy and tolerability. *Expert Opin Drug Metab Toxicol* 2008; **4:** 287–304.

Administration in renal impairment. Patients with renal impairment have an increased risk of developing myopathy and statins should be used with caution, particularly in higher doses. In severe renal impairment plasma-rosuvastatin concentrations may be increased and dosage reduction may be necessary.

UK licensed product information recommends the following oral doses according to creatinine clearance (CC):

- CC 30 to 60 mL/minute: initial oral dose of 5 mg once daily and a maximum dose of 20 mg once daily
- CC below 30 mL/minute: contra-indicated

In the USA usual doses (see above) are allowed in moderate impairment but an initial dose of 5 mg once daily and a maximum dose of 10 mg once daily is recommended in those with CC below 30 mL/minute per 1.73 m^2.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Crestor; Rosuvast; Rovartal; Sinlip; ***Austral.:*** Crestor; ***Austria:*** Crestor; ***Belg.:*** Crestor; ***Braz.:*** Vivacor; ***Canad.:*** Crestor; ***Chile:*** Cresadex; Crestor; Rosumed; ***Cz.:*** Crestor; ***Denm.:*** Crestor; ***Fin.:*** Crestor; ***Fr.:*** Crestor; ***Gr.:*** Crestor; ***Hong Kong:*** Crestor; ***Hung.:*** Crestor; ***India:*** Razel†; Rosuvas; ***Indon.:*** Crestor; ***Irl.:*** Crestor; ***Israel:*** Crestor; ***Ital.:*** Crestor; Provisacor; Simestat; ***Jpn:*** Crestor; ***Malaysia:*** Crestor; ***Mex.:*** Crestor; ***Neth.:*** Cirantan; Crestor; Provisacor; ***Philipp.:*** Crestor; ***Port.:*** Crestor; Visacor; ***Rus.:*** Crestor (Крестор); ***S.Afr.:*** Crestor; ***Singapore:*** Crestor; ***Swed.:*** Crestor; ***Thai.:*** Crestor; ***UK:*** Crestor; ***USA:*** Crestor; ***Venez.:*** Crestor.

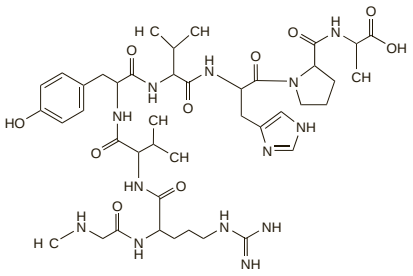
Saralasin Acetate *(BANM, USAN, rINNM)*

Acetato de sarasalina; P-113; Saralasine, Acétate de; Saralasini Acetas; The acetate of 1-Sar-8-Ala-angiotensin II. The hydrated acetate of Sar-Arg-Val-Tyr-Val-His-Pro-Ala; [1-(*N*-Methylglycine)-5-L-valine-8-L-alanine]-angiotensin II acetate hydrate.

Саралазина Ацетат

$C_{42}H_{65}N_{13}O_{10}$, xCH_3COOH,xH_2O = 912.0 (saralasin).

CAS — 34273-10-4 (saralasin); 54194-01-3 (anhydrous saralasin); 39698-78-7 (saralasin acetate hydrate).



(saralasin)

Profile

Saralasin acetate is a competitive antagonist of angiotensin II and thus blocks its pressor action. It is also a partial agonist and causes a transient initial rise in blood pressure. Saralasin has a short half-life and has been used in the differential diagnosis of renovascular hypertension but its use has largely been superseded.

Sarpogrelate Hydrochloride *(rINNM)*

Hidrocloruro de sarpogrelato; MCI-9042; Sarpogrélate, Chlorhydrate de; Sarpogrelati Hydrochloridum. (±)-2-(Dimethylamino)-1-{[o-(*m*-methoxyphenethyl)phenoxy]methyl}ethyl hydrogen succinate hydrochloride.

Сарпогрелата Гидрохлорид

$C_{24}H_{31}NO_6$,HCl = 466.0.

CAS — 125926-17-2 (sarpogrelate); 135159-51-2 (sarpogrelate hydrochloride).

Profile

Sarpogrelate is a serotonin 5-HT_2-receptor antagonist used as an inhibitor of platelet aggregation in thromboembolic disorders. It is given for occlusive arterial disease (see Peripheral Vascular Disease, p.1178) in oral doses of 100 mg of the hydrochloride three times daily.

Preparations

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

Saruplase *(BAN, rINN)*

Prourokinase, Non-glycosylated; Recombinant Human Single-Chain Urokinase-type Plasminogen Activator; Saruplasa; Saruplasum; scuPA. Prourokinase (enzyme-activating) (human clone pUK4/pUK18), non-glycosylated.

Саруплаза

$C_{2031}H_{3121}N_{585}O_{601}S_{31}$ = 46343.1.

CAS — 99149-95-8.
ATC — B01AD08.
ATC Vet — QB01AD08.

NOTE. The term prourokinase has been used for both saruplase and nasaruplase (p.1346).

Profile

Saruplase is a thrombolytic drug. It is a urokinase-type plasminogen activator with a single chain structure prepared via recombinant DNA technology and is converted to urokinase (p.1420) in the body by plasmin. It also has some intrinsic plasminogen-activating properties. Saruplase has been investigated in acute myocardial infarction.

◊ References.

1. Tebbe U, *et al.* Randomized, double-blind study comparing saruplase with streptokinase therapy in acute myocardial infarction: the COMPASS equivalence trial. *J Am Coll Cardiol* 1998; **31:** 487–93.

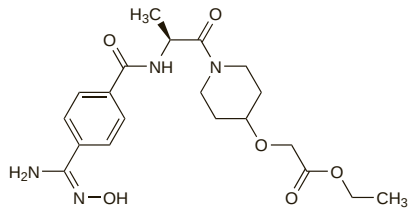
Sibrafiban *(BAN, USAN, rINN)*

G-7333; Ro-48-3657/001; Sibrafibán; Sibrafibanum. Ethyl (*Z*)-[(1-{*N*-[(*p*-hydroxyamidino)benzoyl]-L-alanyl}-4-piperidyl)oxy] acetate.

Сибрафибан

$C_{20}H_{28}N_4O_6$ = 420.5.

CAS — 172927-65-0.



Profile

Sibrafiban is a glycoprotein IIb/IIIa-receptor antagonist. It has been investigated as an oral antiplatelet drug in unstable angina and myocardial infarction but results have been disappointing.

◊ References.

1. Cannon CP, *et al.* Randomized trial of an oral platelet glycoprotein IIb/IIIa antagonist, sibrafiban, in patients after an acute coronary syndrome: results of the TIMI 12 trial. *Circulation* 1998; **97:** 340–9.
2. The SYMPHONY Investigators. Comparison of sibrafiban with aspirin for prevention of cardiovascular events after acute coronary syndromes: a randomised trial. *Lancet* 2000; **355:** 337–45.
3. Second SYMPHONY Investigators. Randomized trial of aspirin, sibrafiban, or both for secondary prevention after acute coronary syndromes. *Circulation* 2001; **103:** 1727–33.

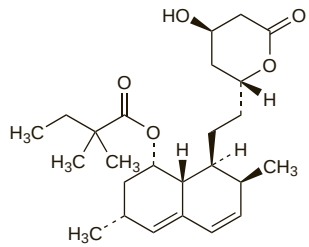
Simvastatin *(BAN, USAN, rINN)*

L-644128-000U; MK-733; Simvastatiini; Simvastatina; Simvastatinas; Simvastatine; Simvastatinum; Sinvinolina; Synvinolin; Szimvasztatin; Velastatin; Velastatina. (1*S*,3*R*,7*S*,8*S*,8a*R*)-1,2,3,7,8,8a-Hexahydro-3,7-dimethyl-8-{2-[(2*R*,4*R*)-tetrahydro-4-hydroxy-6-oxo-2*H*-pyran-2-yl]ethyl}-1-naphthyl 2,2-dimethylbutyrate.

Симвастатин

$C_{25}H_{38}O_5$ = 418.6.

CAS — 79902-63-9.
ATC — C10AA01.
ATC Vet — QC10AA01.



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

Ph. Eur. 6.2 (Simvastatin). A white or almost white crystalline powder. Practically insoluble in water; freely soluble in alcohol; very soluble in dichloromethane. Store under nitrogen in airtight containers. Protect from light.

USP 31 (Simvastatin). A white to off-white powder. Practically insoluble in water; freely soluble in alcohol, in chloroform, and in methyl alcohol; sparingly soluble in propylene glycol; very slightly soluble in petroleum spirit. Store at a temperature between 15° and 30°, or at 2° to 8°.

Adverse Effects

The commonest adverse effects of therapy with simvastatin and other statins are gastrointestinal disturbances. Other adverse effects reported include headache, skin rashes, dizziness, blurred vision, insomnia, and dysgeusia. Reversible increases in serum-aminotransferase concentrations may occur and liver function should be monitored (see Precautions, below). Hepatitis and pancreatitis have been reported. Hypersensitivity reactions including anaphylaxis and angioedema have also occurred. Myopathy, characterised by myalgia and muscle weakness and associated with increased creatine phosphokinase concentrations, has been reported, especially in patients also taking ciclosporin, fibric acid derivatives, or nicotinic acid. Rarely, rhabdomyolysis with acute renal failure may develop.

◊ General references.

1. Farmer JA, Torre-Amione G. Comparative tolerability of the HMG-CoA reductase inhibitors. *Drug Safety* 2000; **23:** 197–213.
2. Davidson MH. Safety profiles for the HMG-CoA reductase inhibitors: treatment and trust. *Drugs* 2001; **61:** 197–206.
3. Pasternak RC, *et al.* ACC/AHA/NHLBI clinical advisory on the use and safety of statins. *Circulation* 2002; **106:** 1024–8. Also available at: http://circ.ahajournals.org/cgi/reprint/106/8/1024.pdf (accessed 29/05/08)
4. Karthikeyan VJ. Adverse effects of statins: an update. *Adverse Drug React Bull* 2005; (Aug): 895–8.
5. McKenney JM, *et al.* Final conclusions and recommendations of the National Lipid Association Statin Safety Assessment Task Force. *Am J Cardiol* 2006; **97** (Issue 8 suppl 1): 89C–94C.
6. Armitage J. The safety of statins in clinical practice. *Lancet* 2007; **370:** 1781–90.

Incidence of adverse effects. By February 1992 the UK CSM had received 738 reports of adverse effects associated with simvastatin,[1] from an estimated 257 000 prescriptions. Abnormal hepatic function and myalgia were 2 of the most frequently reported reactions, with 36 and 48 reports respectively, including 5 reports of hepatitis and 2 of jaundice. Other muscle effects included 3 reports of myositis, 10 of myopathy, and 7 reports of asymptomatic increases in serum creatine kinase concentrations. Gastrointestinal adverse effects accounted for 20% of the reports; skin, neurological and musculoskeletal effects for 15% each; psychiatric effects for 10%; liver effects for 7%; and visual effects for 4%. A systematic review[2] of data from clinical studies confirmed that the risk of liver transaminase elevation was increased by statins but there was no significant increase in the incidence of myalgia (reported in about 15% of patients), creatine kinase elevation (0.9%), or rhabdomyolysis (0.2%), compared with placebo. The incidence of adverse effects may be greater with high-dose therapy.[3,4]

1. Committee on Safety of Medicines. Simvastatin. *Current Problems 33* 1992. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024451&RevisionSelectionMethod=LatestReleased (accessed 30/05/08)
2. Kashani A, *et al.* Risks associated with statin therapy: a systematic overview of randomized clinical trials. *Circulation* 2006; **114:** 2788–97.
3. Davidson MH, Robinson JG. Safety of aggressive lipid management. *J Am Coll Cardiol* 2007; **49:** 1753–62.
4. Silva M, *et al.* Meta-analysis of drug-induced adverse events associated with intensive-dose statin therapy. *Clin Ther* 2007; **29:** 253–60.

Carcinogenicity. For discussion of the effects of statins on the risk of cancer, see Malignant Neoplasms under Uses, below.

Effects on the blood. *Thrombocytopenia* has been reported rarely with statin therapy. Serious thrombocytopenic purpura has occurred with simvastatin, with the onset ranging from 1 or 2 days[1,2] to 11 or 12 months[3,4] after starting treatment. Platelet counts improved after stopping simvastatin in each case, although most patients were given corticosteroids, immunoglobulins, or plasma exchange. There has also been a similar report with atorvastatin,[5] which recurred on rechallenge; the patient had previously taken simvastatin without developing thrombocytopenia, suggesting an idiosyncratic reaction.

A case of *haemolytic anaemia* has been reported[6] in a patient taking lovastatin; no adverse effect was seen when the patient was given simvastatin.

Statins have effects on coagulation and fibrinolysis but these are generally beneficial (see Action under Uses, below); there have been rare reports of *ocular haemorrhage*,[7] but the association with statins is not established.

1. McCarthy LJ, *et al.* Thrombotic thrombocytopenic purpura and simvastatin. *Lancet* 1998; **352:** 1284–5.
2. Sundram F, *et al.* Thrombotic thrombocytopenic purpura associated with statin treatment. *Postgrad Med J* 2004; **80:** 551–2.
3. Possamai G, *et al.* Thrombocytopenic purpura during therapy with simvastatin. *Haematologica* 1992; **77:** 357–8.
4. Groneberg DA, *et al.* Simvastatin-induced thrombocytopenia. *Am J Hematol* 2001; **67:** 277.
5. González-Ponte ML, *et al.* Atorvastatin-induced severe thrombocytopenia. *Lancet* 1998; **352:** 1284.
6. Robbins MJ, *et al.* Lovastatin-induced hemolytic anemia: not a class-specific reaction. *Am J Med* 1995; **99:** 328–9.
7. Fraunfelder FW. Ocular hemorrhage possibly the result of HMG-CoA reductase inhibitors. *J Ocul Pharmacol Ther* 2004; **20:** 179–82.

Effects on the eyes. Studies in *animals* have suggested that some statins could cause cataracts, but this has not been confirmed in humans. Although a study[1] with lovastatin found lens opacities in 13 of 101 patients after treatment for 18 weeks, no deterioration in visual function was found in 11 of these who continued lovastatin and were followed up for an average of 26 months from the start of treatment. Similarly, no differences were found in the development of lens opacities or in changes in visual acuity between patients treated with lovastatin for 48 weeks and patients taking placebo in a study of 8245 patients.[2] A large case-control study[3] found no evidence that use of therapeutic statin doses was associated with the development of cataracts, although the risk did appear to be increased in patients taking simvastatin with erythromycin. Further observational studies have suggested that statins may have beneficial effects; in one study[4] there was no effect on the overall incidence of cataract but the risk of developing nuclear cataract appeared to be decreased, while another study[5] reported a reduction in the overall incidence but this was not significant for any specific cataract type.

For mention of ocular haemorrhage in patients taking statins, see above.

1. Hunninghake DB, *et al.* Lovastatin: follow-up ophthalmologic data. *JAMA* 1988; **259:** 354–5.