Raynaud's syndrome. ACE inhibitors are among many drugs that have been tried in Raynaud's syndrome, a vasospastic peripheral vascular disease (p.1178). Variable effects have been reported. In a patient with Raynaud's syndrome captopril improved blood circulation in the fingers both acutely and during long-term therapy with a dose of 37.5 mg daily; the effect was apparently related to its effects on kinins rather than inhibition of angiotensin II formation.[1] However, a double-blind crossover study in 15 patients with Raynaud's phenomenon given captopril 25 mg or placebo three times daily for 6 weeks found that the drug improved blood flow but not the frequency or severity of attacks,[2] and a similar study in patients given enalapril failed to find any subjective or objective benefits.[3]

There has also been a report[4] of a patient in whom peripheral ischaemia induced by ergotamine was rapidly reversed by captopril.

1. Miyazaki S, *et al.* Relief from digital vasospasm by treatment with captopril and its complete inhibition by serine proteinase inhibitors in Raynaud's phenomenon. *BMJ* 1982; **284:** 310–11.
2. Rustin MHA, *et al.* The effect of captopril on cutaneous blood flow in patients with primary Raynaud's phenomenon. *Br J Dermatol* 1987; **117:** 751–8.
3. Challenor VF, *et al.* Subjective and objective assessment of enalapril in primary Raynaud's phenomenon. *Br J Clin Pharmacol* 1991; **31:** 477–80.
4. Zimran A, *et al.* Treatment with captopril for peripheral ischaemia induced by ergotamine. *BMJ* 1984; **288:** 364.

Stroke. Antihypertensive therapy reduces the risk of stroke (p.1185) in patients with hypertension. However, in patients who have had a stroke, antihypertensive therapy has often been avoided due to the perceived risk of reducing cerebral perfusion. A study[1] of blood-pressure lowering with the ACE inhibitor perindopril, alone or with a diuretic, found that the risk of recurrent stroke was reduced in patients with a history of stroke or transient ischaemic attack, irrespective of whether they had a normal or raised blood pressure at study entry. Retrospective studies[2,3] have also suggested that stroke severity may be reduced in patients who are already taking ACE inhibitors. The beneficial effects of ACE inhibitors in stroke may not be entirely due to their antihypertensive effects; in the HOPE study,[4] ramipril reduced the incidence of stroke in patients with high cardiovascular risk despite only a small reduction in blood pressure.

There have also been reports[5,6] that ACE inhibitors may reduce the risk of pneumonia in patients with a history of stroke, possibly by an effect on symptomless dysphagia.[7]

1. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001; **358:** 1033–41. Corrections. *ibid.*; 1556 and 2002; **359:** 2120.
2. Kumar S, *et al.* Antiplatelets, ACE inhibitors, and statins combination reduces stroke severity and tissue at risk. *Neurology* 2006; **66:** 1153–8.
3. Chitravas N, *et al.* Is prestroke use of angiotensin-converting enzyme inhibitors associated with better outcome? *Neurology* 2007; **68:** 1687–93.
4. Bosch J, *et al.* Use of ramipril in preventing stroke: double blind randomised trial. *BMJ* 2002; **324:** 699–702.
5. Sekizawa K, *et al.* ACE inhibitors and pneumonia. *Lancet* 1998; **352:** 1069.
6. Arai T, *et al.* ACE inhibitors and pneumonia in elderly people. *Lancet* 1998; **352:** 1937–8.
7. Arai T, *et al.* ACE inhibitors and symptomless dysphagia. *Lancet* 1998; **352:** 115–6.

Acebutolol *(BAN, USAN, rINN)* ⊗

Acébutolol; Acebutololum; Asebutolol; Asebutololi. (±)-3′-Acetyl-4′-(2-hydroxy-3-isopropylaminopropoxy)butyranilide.

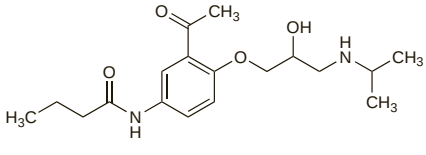
Ацебутолол

$C_{18}H_{28}N_2O_4$ = 336.4.

CAS — 37517-30-9.

ATC — C07AB04.

ATC Vet — QC07AB04.



Acebutolol Hydrochloride *(BANM, rINNM)* ⊗

Acébutolol, chlorhydrate d'; Acebutolol-hidroklorid; Acebutolol-hydrochlorid; Acebutololhydroklorid; Acebutololi hydrochloridum; Acebutololio hidrochloridas; Acebutololu chlorowodorek; Asebutololihydrokloridi; Hidrocloruro de acebutolol; IL-17803A; M&B-17803A.

Ацебутолола Гидрохлорид

$C_{18}H_{28}N_2O_4$,HCl = 372.9.

CAS — 34381-68-5.

ATC — C07AB04.

ATC Vet — QC07AB04.

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

Ph. Eur. 6.2 (Acebutolol Hydrochloride). A white or almost white crystalline powder. Freely soluble in water and in alcohol; very slightly soluble in acetone and in dichloromethane. A 1% solution in water has a pH of 5.0 to 7.0. Protect from light.

USP 31 (Acebutolol Hydrochloride). A white or almost white crystalline powder. Soluble in water and in alcohol; very slightly soluble in acetone and in dichloromethane; practically insoluble in ether. pH of a 1% solution in water is between 4.5 and 7.0. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Breast feeding. Concentrations of acebutolol and its active metabolite diacetolol in breast milk are higher than those in maternal plasma.[1] Pharmacological effects in the neonate, including hypotension, bradycardia, and tachypnoea, have been reported,[1] and the American Academy of Pediatrics therefore considers[2] that acebutolol should be given with caution to breast-feeding mothers.

1. Boutroy MJ, *et al.* To nurse when receiving acebutolol: is it dangerous for the neonate? *Eur J Clin Pharmacol* 1986; **30:** 737–9.
2. 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 liver. Six cases of hepatotoxicity associated with acebutolol were reported[1] in the USA to the FDA between 1985 and 1989. The syndrome consisted of markedly elevated transaminase concentrations, moderately elevated alkaline phosphatase concentrations, and other constitutional symptoms such as fever, nausea, abdominal pain, and headache. The duration of therapy before onset of symptoms ranged from 10 to 31 days; 5 patients received a daily dose of 400 mg; the dose was unspecified in the sixth patient. The syndrome resolved when acebutolol was stopped but reappeared in 2 patients who were rechallenged.

1. Tanner LA, *et al.* Hepatic toxicity after acebutolol therapy. *Ann Intern Med* 1989; **111:** 533–4.

Effects on respiratory function. Bronchospasm is a recognised adverse effect of beta blockers, but other respiratory disorders have also been reported. Pleurisy and pulmonary granulomas developed in a patient given acebutolol and a diuretic; acebutolol was considered to be responsible.[1] Hypersensitivity pneumonitis has also been reported in a patient taking acebutolol.[2]

1. Wood GM, *et al.* Pleurisy and pulmonary granulomas after treatment with acebutolol. *BMJ* 1982; **285:** 936.
2. Akoun GM, *et al.* Acebutolol-induced hypersensitivity pneumonitis. *BMJ* 1983; **286:** 266–7.

Hypersensitivity. See Effects on Respiratory Function, above and Lupus, below.

Lupus. An increase in antinuclear antibodies has been seen with acebutolol.[1] A report of a lupus syndrome in an elderly patient given acebutolol and clonidine described remission of symptoms when acebutolol was withdrawn, but the high antinuclear antibody titre persisted for more than 9 months.[2] Acebutolol was also reported to have caused subacute cutaneous lupus erythematosus in a 57-year-old woman. The condition had resolved completely 4 months after acebutolol was stopped.[3] The authors noted that there had been 9 previous reports of lupus in patients taking acebutolol, but only one had skin manifestations.

1. Wilson JD. Antinuclear antibodies and cardiovascular drugs. *Drugs* 1980; **19:** 292–305.
2. Hourdebaigt-Larrusse P, *et al.* Une nouvelle observation de lupus induit par acébutolol. *Ann Cardiol Angeiol (Paris)* 1985; **34:** 421–3.
3. Fenniche S,*et al.* Acebutolol-induced subacute cutaneous lupus erythematosus. *Skin Pharmacol Physiol* 2005; **18:** 230–3.

Pregnancy. Both acebutolol and its active metabolite diacetolol cross the placenta. In a study[1] in 29 pregnant women who had received acebutolol for at least one month before delivery, there was evidence of bradycardia in 12 of the 31 offspring and tachypnoea in 6.

1. Boutroy MJ, *et al.* Infants born to hypertensive mothers treated by acebutolol. *Dev Pharmacol Ther* 1982; **4** (suppl 1): 109–15.

Interactions

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

Pharmacokinetics

Acebutolol is well absorbed from the gastrointestinal tract, but undergoes extensive first-pass metabolism in the liver. Although the bioavailability of acebutolol is reported to be only about 40%, the major metabolite diacetolol is active. After oral doses, peak plasma concentrations of acebutolol and diacetolol are reached in about 2 and 4 hours, respectively.

Acebutolol and diacetolol are widely distributed in the body, but they have low to moderate lipid solubility and penetration into the CSF is poor. They cross the placenta and higher concentrations are achieved in breast milk than in maternal plasma. Acebutolol is only about 26% bound to plasma proteins, but is about 50% bound to erythrocytes. The plasma elimination half-lives for acebutolol and diacetolol are 3 to 4 hours and 8 to 13 hours respectively. Half-life values for acebutolol and diacetolol may be increased in the elderly and the half-life for diacetolol may be prolonged up to 32 hours in patients with severe renal impairment. Acebutolol and diacetolol are excreted in the urine and in the bile and may undergo enterohepatic recycling; acebutolol is also reported to be excreted directly from the intestinal wall, and more than 50% of an oral dose can be recovered from the faeces. Acebutolol and diacetolol are removed by dialysis.

Uses and Administration

Acebutolol is a cardioselective beta blocker (p.1225). It is reported to have some intrinsic sympathomimetic activity and membrane stabilising properties.

Acebutolol is used in the management of hypertension (p.1171), angina pectoris (p.1157), and cardiac arrhythmias (p.1160).

Acebutolol is used as the hydrochloride, but doses are usually expressed in terms of the base; 110.8 mg of acebutolol hydrochloride is equivalent to 100 mg of base. It is generally given orally although slow intravenous injection has been used for the emergency treatment of arrhythmias.

In **hypertension** the usual initial oral dose is 400 mg once daily or 200 mg twice daily, increased if necessary after 2 weeks to 400 mg twice daily. Doses up to 1.2 g daily in divided doses may be given.

The usual oral dose for **angina pectoris** is 400 mg once daily or 200 mg twice daily, but up to 300 mg three times daily may be required for severe cases and total daily doses of 1.2 g have been given.

The usual initial oral dose for **cardiac arrhythmias** is 200 mg twice daily, increased according to response; up to 1.2 g daily in divided doses has been required.

Reduced doses may be required in patients with impaired renal function (see below). Elderly patients may also require lower maintenance doses; doses greater than 800 mg daily should be avoided.

Action. Acebutolol is generally considered to be a cardioselective beta blocker but there has been considerable controversy as to the degree of its selectivity and the selectivity of its primary metabolite, diacetolol.[1-3] In a review of beta blockers,[4] acebutolol was stated to be less cardioselective than other drugs such as atenolol or metoprolol. It was proposed[5] that this may be because the metabolite accumulates during chronic dosage to reach concentrations that affect both $beta_1$ and $beta_2$ receptors since cardioselectivity is only a relative and dose-related phenomenon. This remains uncertain and there is some evidence[6] that at least after single doses, diacetolol is actually more cardioselective than acebutolol itself.

1. Whitsett TL, *et al.* Comparison of the beta and beta adrenoceptor blocking properties of acebutolol and propranolol. *Chest* 1982; **82:** 668–73.
2. Nair S, *et al.* The effect of acebutolol, a beta adrenergic blocking agent, and placebo on pulmonary functions in asthmatics. *Int J Clin Pharmacol Ther Toxicol* 1981; **19:** 519–26.
3. Leary WP, *et al.* Respiratory effects of acebutolol hydrochloride: a new selective beta-adrenergic blocking agent. *S Afr Med J* 1973; **47:** 1245–8.
4. Feely J, *et al.* Beta-blockers and sympathomimetics. *BMJ* 1983; **286:** 1043–7.
5. Feely J, Maclean D. New drugs: beta blockers and sympathomimetics. *BMJ* 1983; **286:** 1972.
6. Thomas MS, Tattersfield AE. Comparison of beta-adrenoceptor selectivity of acebutolol and its metabolite diacetolol with metoprolol and propranolol in normal man. *Eur J Clin Pharmacol* 1986; **29:** 679–83.

Administration in renal impairment. The dose of acebutolol should be reduced in patients with renal impairment. It is recommended that the dose should be reduced by 50% in patients with a creatinine clearance between 25 and 50 mL/minute and by 75% in those with a creatinine clearance of less than 25 mL/minute. The dose frequency should not exceed once daily.

Preparations

BP 2008: Acebutolol Capsules; Acebutolol Tablets;
USP 31: Acebutolol Hydrochloride Capsules.

Proprietary Preparations (details are given in Part 3)
Belg.: Sectral; ***Canad.:*** Monitan; Rhotral; Sectral; ***Chile:*** Beloc; Grifobutol; ***Cz.:*** Acecor; Apo-Acebutol; Sectral; ***Denm.:*** Diasectral; ***Fin.:*** Diasectral; Espesil; ***Fr.:*** Sectral; ***Ger.:*** Prent; ***Hong Kong:*** Sectral; ***Irl.:*** Sectral†; ***Israel:*** Sectral; ***Ital.:*** Prent; Sectral; ***Malaysia:*** Sectral†; ***Neth.:*** Sectral; ***NZ:*** ACB; ***Pol.:*** Abutol; Sectral; ***Port.:*** Prent; ***S.Afr.:*** Butobloc; Sectral; ***Singapore:*** ACB†; Sectral; ***Spain:*** Sectral†; ***Switz.:*** Sectral†; ***Turk.:*** Prent; ***UK:*** Sectral; ***USA:*** Sectral; ***Venez.:*** Flebutol†.

Multi-ingredient: ***Belg.:*** Sectrazide; ***Ger.:*** Sali-Prent; Tredalat; ***Indon.:*** Sectrazide; ***Neth.:*** Secadrex†; ***Spain:*** Secadrex†; ***UK:*** Secadrex†.

Acenocoumarol *(BAN, rINN)*

Acénocoumarol; Acenocoumarolum; Acenocumarin; Acenocumarol; Acenokumarol; Asenokumarol; G-23350; Nicoumalone; Nikumalon. (*RS*)-4-Hydroxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-coumarin.

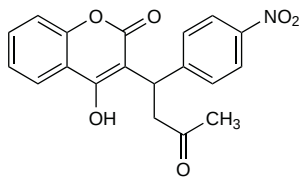
Аценокумарол

$C_{19}H_{15}NO_6$ = 353.3.

CAS — 152-72-7.

ATC — B01AA07.

ATC Vet — QB01AA07.



Pharmacopoeias. In *Br.* and *Pol.*
BP 2008 (Acenocoumarol). An almost white to buff-coloured odourless or almost odourless powder. It exhibits polymorphism. Practically insoluble in water and in ether; slightly soluble in alcohol and in chloroform; dissolves in aqueous solutions of alkali hydroxides.

Adverse Effects, Treatment, and Precautions

As for Warfarin Sodium, p.1425.

Effects on the fetus. In a group of women who received acenocoumarol for anticoagulant prophylaxis of mechanical heart valves during pregnancy,[1] fetal loss occurred in 13 of 61 pregnancies where oral anticoagulation was continued during the first trimester. Apart from 1 case of hydrocephalus no malformations were reported in the remaining neonates.

1. Meschengieser SS, *et al.* Anticoagulation in pregnant women with mechanical heart valve prostheses. *Heart* 1999; **82:** 23–6.

Interactions

The interactions associated with oral anticoagulants are discussed in detail under warfarin (p.1427). Specific references to interactions involving acenocoumarol can be found there under the headings for the following drug groups: analgesics; antiarrhythmics; antibacterials; antidepressants; antifungals; antigout drugs; antihistamines; antineoplastics; antiplatelets; antivirals; diuretics; gastrointestinal drugs; immunosuppressants; lipid regulating drugs; sex hormones; and vaccines.

Pharmacokinetics

Acenocoumarol is readily absorbed from the gastrointestinal tract and is excreted chiefly in the urine mainly as metabolites. It is extensively bound to plasma proteins. Figures reported for elimination half-life vary; UK licensed product information gives a range of 8 to 11 hours. Acenocoumarol crosses the placenta; only small quantities have been detected in breast milk. It is given as a racemic mixture; the *R*-isomer is more potent. The stereo-isomers have different pharmacokinetics. Metabolism of the *S*-isomer is mediated mainly by the cytochrome P450 isoenzyme CYP2C9, which shows genetic polymorphism; other isoenzymes as well are involved in the metabolism of the *R*-isomer.

◊ References.

1. Ufer M. Comparative pharmacokinetics of vitamin K antagonists: warfarin, phenprocoumon and acenocoumarol. *Clin Pharmacokinet* 2005; **44:** 1227–46.

Uses and Administration

Acenocoumarol is an oral coumarin anticoagulant with actions similar to those of warfarin (p.1432). It is used in the management of thromboembolic disorders (p.1187). The usual dose is 4 to 12 mg on the first day and 4 to 8 mg on the second day; subsequent maintenance doses range from 1 to 8 mg depending on the response. Acenocoumarol is given in a single dose at the same time every day.

Preparations

BP 2008: Acenocoumarol Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Acenotromb; Antitrom; Azecar; Cumarol; Fortonol; Saxion; Sintrom; ***Austria:*** Sintrom; ***Belg.:*** Sintrom; ***Canad.:*** Sintrom; ***Chile:*** Acenox; Coarol; Isquelium; Neo-Sintrom; ***Fr.:*** Mini-sintrom; Sintrom; ***Gr.:*** Sintrom; ***Hung.:*** Syncumar; ***India:*** Acitrom; ***Israel:*** Sintrom; ***Ital.:*** Sintrom; ***Mex.:*** Sintrom; ***Neth.:*** Sintrom Mitis; ***Pol.:*** Sintrom; Syncumar; ***Port.:*** Sintrom; ***Spain:*** Sintrom; ***Switz.:*** Sintrom; ***UK:*** Sinthrome.

Acetyldigoxin

Acetildigoxina; Acetyldigoxin-beta; Acetyldigoxinum; β-Acetyldigoxinum; Acetyldigoxinum Beta; β-Acetylodigoksyna; Asetyylidigoksiini; Desglucolanatoside C. 3β-[(*O*-3-*O*-Acetyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12β,-14-dihydroxy-5β,14β-card-20(22)-enolide (α-acetyldigoxin); 3β-[(*O*-4-*O*-Acetyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12β,14-dihydroxy-5β,14β-card-20(22)-enolide (β-acetyldigoxin).

$C_{43}H_{66}O_{15}$ = 823.0.

CAS — 5511-98-8 (α-acetyldigoxin); 5355-48-6 (β-acetyldigoxin).

ATC — C01AA02.

ATC Vet — QC01AA02.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (β-Acetyldigoxin). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol; sparingly soluble in dichloromethane. Protect from light.

Profile

Acetyldigoxin is a cardiac glycoside with positive inotropic activity. It has the general properties of digoxin (p.1259) and has been used similarly in the management of some cardiac arrhythmias (p.1160) and in heart failure (p.1165). Usual oral maintenance doses for the β-isomer are 200 to 400 micrograms daily; the α-isomer has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Corotal; Lanatilin; Novodigal; ***Ger.:*** Digostada; Digotab; Digox; Digoxin "Didier"†; Novodigal; Stillacor; ***Ital.:*** Cardioreg†.

Multi-ingredient: ***Austria:*** Digi-Aldopur; Gladixol.

Acipimox *(BAN, rINN)*

Acipimoxum; Asipimoks; Asipimoksi; K-9321. 5-Methylpyrazine-2-carboxylic acid 4-oxide.

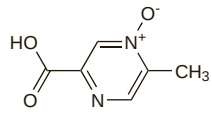
Аципимокс

$C_6H_6N_2O_3$ = 154.1.

CAS — 51037-30-0.

ATC — C10AD06.

ATC Vet — QC10AD06.



Adverse Effects and Precautions

Acipimox may cause peripheral vasodilatation resulting in flushing, itching, and a sensation of heat. Rash and erythema may occur. Gastrointestinal disturbances including heartburn, epigastric pain, nausea, and diarrhoea have been reported, as well as headache, malaise, myalgia, myositis, arthralgia, and dry eye. Urticaria, angioedema, and bronchospasm may occur rarely.

Acipimox is contra-indicated in patients with peptic ulcer disease. It should be used with caution in renal impairment.

Incidence of adverse effects. In a study involving 3009 hyperlipidaemic patients with type 2 diabetes,[1] adverse effects associated with acipimox occurred in 8.8%, resulting in withdrawal in 5.5% of patients. The most frequent adverse effects involved the skin (57.6%), gastrointestinal tract (25.8%), and CNS (9.7%). Labial oedema occurred in 3 cases and an urticarial eruption, collapse, and dyspnoea in another. The incidence of adverse effects was almost twice as high in females as in males, the difference being mainly due to a greater incidence of flushing, pruritus, and skin rashes. The incidence was not affected by age. There was a mean 15.3% reduction in fasting blood-glucose concentrations and an 8.5% reduction in glycosylated haemoglobin during treatment with acipimox.

1. Lavezzari M, *et al.* Results of a phase IV study carried out with acipimox in type II diabetic patients with concomitant hyperlipoproteinaemia. *J Int Med Res* 1989; **17:** 373–80.

Pharmacokinetics

Acipimox is rapidly and completely absorbed from the gastrointestinal tract and peak plasma concentrations occur within 2 hours. It does not bind to plasma proteins and the plasma half-life is about 2 hours. It is not significantly metabolised and is excreted in the urine, largely unchanged.

Uses and Administration

Acipimox is a lipid regulating drug related to nicotinic acid (p.1957). It is used to reduce cholesterol and triglycerides in the management of hyperlipidaemias (see Action, below), including type IIa, IIb, or IV hyperlipoproteinaemias.

Acipimox is given orally in a usual dose of 250 mg two or three times daily, taken with meals. Doses of up to 1200 mg daily have been used. The dose should be adjusted in renal impairment (see below).

Action. Acipimox is used in the management of hyperlipidaemias (p.1169); it is a derivative of nicotinic acid and has similar effects on plasma lipoproteins but is better tolerated.[1] Its primary action is inhibition of lipolysis, leading to a reduction in circulating free fatty acids and consequently a reduction in very-low-density lipoprotein (VLDL) production in the liver. This results in a reduction of triglycerides, particularly in patients with hypertriglyceridaemia;[2] there may also be a decrease in low-density lipoprotein (LDL)-cholesterol and total cholesterol, and an increase in high-density lipoprotein (HDL)-cholesterol. Similar effects have been reported in patients with mixed hyperlipoproteinaemias, although the reduction of triglycerides and LDL-cholesterol was not significant.[3]

Reduction of free fatty acids by acipimox has a number of other physiological effects that have been utilised. Insulin secretion and sensitivity may be modified, and acipimox has been tried in type 2 diabetes mellitus; it improves plasma lipids and may also reduce blood-glucose concentrations,[4] and has been of benefit in patients with type A insulin resistance.[5] Beneficial effects have also been reported[6] in patients with HIV-associated lipodystrophy and insulin resistance. Growth hormone secretion is stimulated in obese subjects, and acipimox has been used in the investigation of growth hormone disorders.[7] There is also an increase in glucose uptake by the heart, and acipimox has been used to enhance myocardial imaging in ^{18}F-fluorodeoxyglucose positron-emission tomography.[8]

1. Tornvall P, Walldius G. A comparison between nicotinic acid and acipimox in hypertriglyceridaemia—effects on serum lipids, lipoproteins, glucose tolerance and tolerability. *J Intern Med* 1991; **230:** 415–21.
2. Ball MJ, *et al.* Acipimox in the treatment of patients with hyperlipidaemia: a double blind trial. *Eur J Clin Pharmacol* 1986; **31:** 201–4.
3. Otto C, *et al.* Effects of acipimox on haemorheology and plasma lipoproteins in patients with mixed hyperlipoproteinaemia. *Br J Clin Pharmacol* 1998; **46:** 473–8.
4. Lavezzari M, *et al.* Results of a phase IV study carried out with acipimox in type II diabetic patients with concomitant hyperlipoproteinaemia. *J Int Med Res* 1989; **17:** 373–80.
5. Kumar S, *et al.* Suppression of non-esterified fatty acids to treat type A insulin resistance syndrome. *Lancet* 1994; **343:** 1073–4.
6. Hadigan C, *et al.* Inhibition of lipolysis improves insulin sensitivity in protease inhibitor-treated HIV-infected men with fat redistribution. *Am J Clin Nutr* 2003; **77:** 490–4.
7. Cordido F, *et al.* Effect of acute pharmacological reduction of plasma free fatty acids on growth hormone (GH) releasing hormone-induced GH secretion in obese adults with and without hypopituitarism. *J Clin Endocrinol Metab* 1998; **83:** 4350–4.
8. Knuuti MJ, *et al.* Enhancement of myocardial [fluorine-18]fluorodeoxyglucose uptake by a nicotinic acid derivative. *J Nucl Med* 1994; **35:** 989–98.

Administration in renal impairment. Acipimox is contra-indicated in patients with a creatinine clearance below 30 mL/minute. In patients with creatinine clearance between 30 and 60 mL/minute, the interval between doses should be increased.