Pharmacokinetics

Nesiritide is cleared from the circulation by 3 mechanisms: uptake into cells; proteolytic cleavage by endopeptidases; and excretion by the kidneys. It has a biphasic elimination, with a terminal elimination half-life of 18 minutes.

Uses and Administration

Nesiritide is a recombinant brain natriuretic peptide (see p.1347) used in the management of acutely decompensated heart failure (p.1165). It is given intravenously as the citrate, but dosage is expressed in terms of the base. The initial dose of nesiritide is 2 micrograms/kg by intravenous injection over 1 minute, followed by a maintenance infusion of 10 nanograms/kg per minute.

Heart failure. The use of nesiritide in acute decompensated heart failure (p.1165) has been reviewed.[1,2] It may be used for short-term treatment as an alternative to standard intravenous therapy with vasodilators, inotropes, or diuretics, and appears to have no proarrhythmic effects; however, its effects on mortality are controversial (see under Adverse Effects and Precautions, above) and its role in therapy remains unclear. There is some evidence from retrospective studies that it may be safely used in addition to standard therapy[3,4] and may have a role as a more prolonged treatment in patients awaiting cardiac transplantation.[5] Although nesiritide has also been given intermittently for outpatient management of chronic heart failure, this use is not currently recommended.[6]

1. Vichiendilokkul A, *et al.* Nesiritide: a novel approach for acute heart failure. *Ann Pharmacother* 2003; **37:** 247–58.
2. Keating GM, Goa KL. Nesiritide: a review of its use in acute decompensated heart failure. *Drugs* 2003; **63:** 47–70.
3. O'Dell KM, *et al.* Nesiritide for secondary pulmonary hypertension in patients with end-stage heart failure. *Am J Health-Syst Pharm* 2005; **62:** 606–9.
4. Smull DL, Jorde UP. Concomitant use of nesiritide and milrinone in decompensated congestive heart failure. *Am J Health-Syst Pharm* 2005; **62:** 291–5.
5. Witteles R, *et al.* B-type natriuretic peptide is effective therapy before care. *Ann Intern Med* 2004; **141:** 895.
6. Bauer JB, Randazzo MA. Nesiritide for outpatient treatment of heart failure. *Am J Health-Syst Pharm* 2005; **62:** 2639–42.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Natrecor; ***Indon.:*** Natrecor; ***Israel:*** Noratak; ***Switz.:*** Noratak; ***USA:*** Natrecor; ***Venez.:*** Natrecor.

Nicardipine Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de nicardipino; Nicardipine, Chlorhydrate de; Nicardipini Hydrochloridum; Nikardipiinihydrokloridi; Nikardipin Hidroklorür; Nikardipinhydroklorid; RS-69216; RS-69216-XX-07-0; YC-93. 2-[Benzyl(methyl)amino]ethyl methyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate hydrochloride.

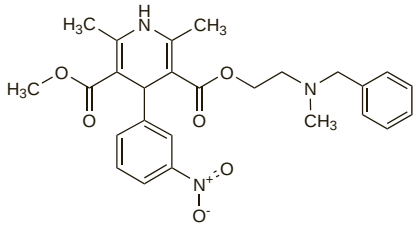
Никардипина Гидрохлорид

$C_{26}H_{29}N_3O_6$,HCl = 516.0.

CAS — 55985-32-5 (nicardipine); 54527-84-3 (nicardipine hydrochloride).

ATC — C08CA04.

ATC Vet — QC08CA04.



(nicardipine)

Pharmacopoeias. In *Chin.* and *Jpn.*

Incompatibility. The manufacturers recommend that a solution containing nicardipine hydrochloride 100 micrograms/mL is used for intravenous infusion. Suitable diluents are solutions of glucose or sodium chloride. Sodium bicarbonate and lactated Ringer's are incompatible with nicardipine infusion. Nicardipine hydrochloride (1 mg/mL in glucose 5%) has also been reported[1] to be visually incompatible with furosemide, heparin, and thiopental.

1. Chiu MF, Schwartz ML. Visual compatibility of injectable drugs used in the intensive care unit. *Am J Health-Syst Pharm* 1997; **54:** 64–5.

Adverse Effects, Treatment, and Precautions

As for dihydropyridine calcium-channel blockers (see Nifedipine, p.1350).

Interactions

As for dihydropyridine calcium-channel blockers (see Nifedipine, p.1352).

Pharmacokinetics

Nicardipine is rapidly and completely absorbed from the gastrointestinal tract but is subject to saturable first-pass hepatic metabolism. Bioavailability of about 35% has been reported after a 30-mg dose at steady state. The pharmacokinetics of nicardipine are non-linear due to the saturable first-pass hepatic metabolism and an increase in dose may produce a disproportionate increase in plasma concentration. There is also considerable interindividual variation in plasma-nicardipine concentrations. Nicardipine is more than 95% bound to plasma proteins. Nicardipine is extensively metabolised in the liver and is excreted in the urine and faeces, mainly as inactive metabolites. The terminal plasma half-life is about 8.6 hours, thus steady-state plasma concentrations are achieved after 2 to 3 days of dosing three times daily.

◊ References.

1. Graham DJM, *et al.* Pharmacokinetics of nicardipine following oral and intravenous administration in man. *Postgrad Med J* 1984; **60** (suppl 4): 7–10.
2. Graham DJM, *et al.* The metabolism and pharmacokinetics of nicardipine hydrochloride in man. *Br J Clin Pharmacol* 1985; **20:** 23S–28S.
3. Razak TA, *et al.* The effect of hepatic cirrhosis on the pharmacokinetics and blood pressure response to nicardipine. *Clin Pharmacol Ther* 1990; **47:** 463–9.
4. Porchet HC, Dayer P. Serum concentrations and effects of (±)-nicardipine compared with nifedipine in a population of healthy subjects. *Clin Pharmacol Ther* 1990; **48:** 155–60.

Uses and Administration

Nicardipine is a dihydropyridine calcium-channel blocker with actions and uses similar to nifedipine (p.1354). It is used in the management of hypertension (p.1171) and angina pectoris (p.1157).

Nicardipine hydrochloride is generally given orally although the intravenous route has been used for the short-term treatment of hypertension.

Oral doses of nicardipine hydrochloride are similar for both **hypertension** and **angina**. The initial dose is 20 mg three times daily and may be increased at intervals of at least 3 days until the required effect is achieved. The usual maintenance dose is 30 mg three times daily, but daily doses of between 60 and 120 mg in divided doses may be given. Modified-release preparations of nicardipine hydrochloride for dosage twice daily are also available.

Nicardipine hydrochloride may be given by slow intravenous infusion as a 100 micrograms/mL solution in the short-term treatment of hypertension. An initial infusion rate of 5 mg/hour is recommended, increased, as necessary, up to a maximum of 15 mg/hour and subsequently reduced to 3 mg/hour. For use in children, see below.

Reduced doses of nicardipine hydrochloride and longer dosing intervals may be necessary in patients with hepatic or renal impairment (see below).

◊ Reviews.

1. Curran MP, *et al.* Intravenous nicardipine: its use in the short-term treatment of hypertension and various other indications. *Drugs* 2006; **66:** 1755–82.

Administration in children. Intravenous infusion of nicardipine has been used in both infants and children for the management of hypertension. In studies[1-4] in children aged between 2 days and 17 years, initial doses ranged from 0.2 to 5 micrograms/kg per minute, with maintenance infusions of 0.15 to 6 micrograms/kg per minute. Adverse effects were rare; one study[4] reported adverse effects in 5 of 31 treatment courses, including tachycardia, flushing, palpitations, and hypotension. There has also been a report[5] of the successful use of intravenous infusion of nicardipine in 8 preterm infants (gestational age 28 to 36 weeks). Infusions were given at a dose of 0.5 to 2 micrograms/kg per minute and continued for periods of 3 to 36 days. No hypotension, oedema, or tachycardia were observed.

The *BNFC* suggests that neonates and children up to age 18 years may be given nicardipine hydrochloride by continuous intravenous infusion for the management of hypertensive crises. The initial dose is 500 nanograms/kg per minute, adjusted according to response; the usual maintenance dose is 1 to 4 micrograms/kg per minute, with a maximum dose of 250 micrograms/minute.

1. Treluyer JM, *et al.* Intravenous nicardipine in hypertensive children. *Eur J Pediatr* 1993; **152:** 712–4.
2. Sartori SC, *et al.* Intravenous nicardipine for treatment of systemic hypertension in children. *Pediatrics* 1999; **104** (suppl): 676–7.
3. Tobias JD. Nicardipine to control mean arterial pressure after cardiothoracic surgery in infants and children. *Am J Ther* 2001; **8:** 3–6.
4. Flynn JT, *et al.* Intravenous nicardipine for treatment of severe hypertension in children. *J Pediatr* 2001; **139:** 38–43.
5. Gouyon JB, *et al.* Intravenous nicardipine in hypertensive preterm infants. *Arch Dis Child* 1997; **76:** F126–F127.

Administration in hepatic or renal impairment. Reduced doses of nicardipine hydrochloride and longer dosing intervals may be necessary in patients with hepatic or renal impairment. The US manufacturers recommend an initial dose of 20 mg twice daily by mouth in patients with hepatic impairment.

Cerebrovascular disorders. Nicardipine has been reported to increase cerebral blood flow[1] and use by various routes has been investigated for possible benefit in haemorrhagic[2-5] and ischaemic stroke[6,7] (p.1185), although nimodipine (p.1357) is the dihydropyridine calcium-channel blocker usually used. Nicardipine has also been tried[8] in patients with cerebrovascular insufficiency. However, studies have produced inconclusive results.

1. Savage I, James I. The effect of nicardipine hydrochloride on cerebral blood flow in normotensive volunteers. *Br J Clin Pharmacol* 1986; **21:** 591P–592P.
2. Suzuki M, *et al.* Intrathecal administration of nicardipine hydrochloride to prevent vasospasm in patients with subarachnoid hemorrhage. *Neurosurg Rev* 2001; **24:** 180–4.
3. Kasuya H, *et al.* Efficacy and safety of nicardipine prolonged-release implants for preventing vasospasm in humans. *Stroke* 2002; **33:** 1011–15.
4. Dorhout Mees SM, *et al.* Calcium antagonists for aneurysmal subarachnoid haemorrhage. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 25/07/08).
5. Barth M, *et al.* Effect of nicardipine prolonged-release implants on cerebral vasospasm and clinical outcome after severe aneurysmal subarachnoid hemorrhage: a prospective, randomized, double-blind phase IIa study. *Stroke* 2007; **38:** 330–6.
6. Yao L, Ding D. Effect of nicardipine on somatosensory evoked potentials in patients with acute cerebral infarction. *J Neurol Neurosurg Psychiatry* 1990; **53:** 844–6.
7. Rosenbaum D, *et al.* Early treatment of ischemic stroke with a calcium antagonist. *Stroke* 1991; **22:** 437–41.
8. Silva APE, Diament CK. Nicardipine versus cinnarizine in cerebrovascular insufficiency. *Curr Ther Res* 1988; **43:** 888–99.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Karden; ***Belg.:*** Rydene; ***Fr.:*** Loxen; ***Ger.:*** Antagonil; ***Indon.:*** Perdipine; ***Irl.:*** Cardene†; ***Ital.:*** Bionicard; Cardioten; Cardip; Cordisol†; Lisanirc; Neucor; Nicant†; Nicapress; Nicardal; Nicarpin; Nicaven; Nimicor; Niven†; Perdipina; Ranvil†; Vasodin; ***Jpn:*** Perdipine; ***Malaysia:*** Cardepine; ***Neth.:*** Cardene; ***Philipp.:*** Cardepine; ***Port.:*** Nerdipina; ***Singapore:*** Cardibloc; ***Spain:*** Dagan; Flusemide; Lecibral; Lincil; Lucenfal; Nerdipina; Vasonase; ***Thai.:*** Cardepine; Nerdipine†; ***Turk.:*** Loxen; ***UK:*** Cardene; ***USA:*** Cardene.

Niceritrol *(BAN, rINN)*

Nicéritrol; Niceritrolum; Nikeritroli; PETN. Pentaerythritol tetranicotinate; 2,2-Bis(hydroxymethyl)propane-1,3-diol tetranicotinate.

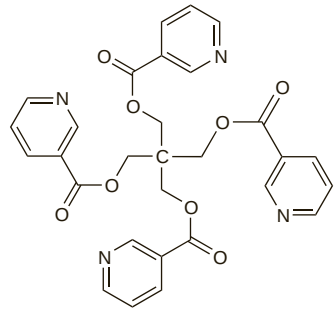
Ницеритрол

$C_{29}H_{24}N_4O_8$ = 556.5.

CAS — 5868-05-3.

ATC — C10AD01.

ATC Vet — QC10AD01.



NOTE. The synonym PETN has been applied to both niceritrol and pentaerithrityl tetranitrate.

Pharmacopoeias. In *Jpn.*

Profile

Niceritrol, an ester of pentaerythritol and nicotinic acid, has general properties similar to those of nicotinic acid (p.1957), to which it is slowly hydrolysed. Niceritrol has been used as a lipid regulating drug in hyperlipidaemias and as a vasodilator in the treatment of peripheral vascular disease.

◊ References.

1. Owada A, *et al.* Antiproteinuric effect of niceritrol, a nicotinic acid derivative, in chronic renal disease with hyperlipidemia: a randomized trial. *Am J Med* 2003; **114:** 347–53.

Nicorandil *(BAN, USAN, rINN)*

Nicorandilum; SG-75. *N*-[2-(Nitroxy)ethyl]-3-pyridinecarboxamide.

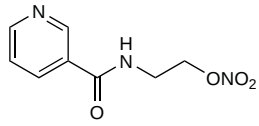
Никорандил

$C_8H_9N_3O_4$ = 211.2.

CAS — 65141-46-0.

ATC — C01DX16.

ATC Vet — QC01DX16.



Pharmacopoeias. In *Jpn.*

Adverse Effects and Precautions

Adverse effects reported with nicorandil are headache (which is usually transitory and seen at the start of therapy), cutaneous vasodilatation and flushing, nausea, vomiting, dizziness, and weakness. Rarely reported effects include myalgia, skin rashes, and oral ulceration, and there have been very rare reports of angioedema and hepatic function abnormalities. A reduction in blood pressure and/or an increase in heart rate may occur with high doses.

Nicorandil is contra-indicated in patients with cardiogenic shock, left ventricular failure with low filling pressures, and hypotension. In patients with hypovolaemia, low systolic blood pressure, acute pulmonary oedema, or acute myocardial infarction with acute left ventricular failure and low filling pressures, nicorandil should preferably be avoided but may be used with caution.

Incidence of adverse effects. Postmarketing surveillance for nicorandil was carried out by prescription-event monitoring[1] of 13 620 patients, and showed that adverse reactions occurred in 175. The most frequent was headache, occurring in 58 patients, mainly in the first month of treatment. Unspecified adverse effects occurred in 36 patients. Other effects included dizziness (19), nausea (17), malaise (13), palpitations (8), flushing and vomiting (6 each), and lassitude (4). Rare adverse effects included 3 cases each of angioedema and photosensitivity.

1. Dunn N, *et al.* Safety profile of nicorandil—prescription-event monitoring (PEM) study. *Pharmacoepidemiol Drug Safety* 1999; **8:** 197–205.

Ulceration. Nicorandil has been associated with ulceration of mucosal surfaces. Painful, large aphthous ulcers on the *tongue* and *oral mucosa* have been reported[1-3] in patients receiving nicorandil for angina. The ulcers were usually resistant to treatment but all healed when nicorandil was withdrawn. Colchicine or thalidomide treatment has improved ulcers associated with nicorandil in a few patients, but relapse occurred when the colchicine or thalidomide was stopped.[3] However, a large study[4] casts some doubt on the evidence for a causal link between nicorandil and oral ulceration, although it was suggested that this could be further investigated.

Anal ulceration has been reported[5-7] in patients taking nicorandil. Healing of the ulcers occurred in those patients in whom nicorandil was withdrawn.

Multiple ulcers of the upper and lower *gastrointestinal tract*, in addition to oral and anal ulceration, have been reported[8] in a patient taking nicorandil; all of the ulcers healed when nicorandil was stopped. There have also been several cases of *peristomal* ulceration, which resolved after stopping nicorandil.[9]

Perivulval ulceration has also been reported, and in 1 case was associated with a *cutaneous* ulcer.[10] Another patient[11] developed both perianal and leg ulcers, both of which improved rapidly when nicorandil was stopped.

1. Cribier B, *et al.* Chronic buccal ulceration induced by nicorandil. *Br J Dermatol* 1998; **138:** 372–3.
2. Desruelles F, *et al.* Giant oral aphthous ulcers induced by nicorandil. *Br J Dermatol* 1998; **138:** 712–13.
3. Agbo-Godeau S, *et al.* Association of major aphthous ulcers and nicorandil. *Lancet* 1998; **352:** 1598–9.
4. Dunn N, *et al.* Safety profile of nicorandil—prescription-event monitoring (PEM) study. *Pharmacoepidemiol Drug Safety* 1999; **8:** 197–205.
5. Watson A, *et al.* Nicorandil associated anal ulceration. *Lancet* 2002; **360:** 546–7.
6. Vella M, Molloy RG. Nicorandil-associated anal ulceration. *Lancet* 2002; **360:** 1979.
7. Passeron T, *et al.* Chronic anal ulceration due to nicorandil. *Br J Dermatol* 2004; **150:** 394–6.
8. Egred M, *et al.* Nicorandil may be associated with gastrointestinal ulceration. *BMJ* 2006; **332:** 889.
9. Ogden S, *et al.* Nicorandil-induced peristomal ulcers: is nicorandil also associated with gastrointestinal fistula formation? *Br J Dermatol* 2007; **156:** 608–9.
10. Claeys A, *et al.* Cutaneous, perivulvar and perianal ulcerations induced by nicorandil. *Br J Dermatol* 2006; **155:** 494–6.
11. McKenna DJ, *et al.* Nicorandil-induced leg ulceration. *Br J Dermatol* 2007; **156:** 394–6.

Interactions

Nicorandil should not be used with phosphodiesterase type-5 inhibitors such as sildenafil as the hypotensive effect of nicorandil may be significantly enhanced.

Pharmacokinetics

Nicorandil is well absorbed from the gastrointestinal tract and maximum plasma concentrations are achieved 30 to 60 minutes after oral doses. Metabolism is mainly by denitration and about 20% of a dose is excreted in the urine mainly as metabolites. The elimination half-life is about 1 hour. Nicorandil is only slightly bound to plasma proteins.

Uses and Administration

Nicorandil is a nitrate derivative of nicotinamide (p.1957) and acts as a vasodilator. It is a potassium-channel opener (p.1155) providing vasodilatation of arterioles and large coronary arteries and its nitrate component produces venous vasodilatation through stimulation of guanylate cyclase. It thus reduces both preload and afterload, and improves coronary blood flow.

Nicorandil is given orally for prevention and long-term treatment of **angina pectoris**, including reduction of the risk of acute coronary events in high-risk patients (p.1157). The usual initial oral dose is 10 mg twice daily (or 5 mg twice daily in patients susceptible to headache), increased as necessary to a maximum of 30 mg twice daily; the usual therapeutic dose is in the range of 10 to 20 mg twice daily.

Nicorandil is also given intravenously in the management of **unstable angina** and **acute heart failure** (p.1165). For unstable angina, a solution containing 100 to 300 micrograms/mL is given by intravenous infusion in a dose of 2 mg/hour, adjusted according to response, to a maximum dose of 6 mg/hour. For acute heart failure, a solution containing 400 to 2500 micrograms/mL is used; the usual dose is 200 micrograms/kg given by intravenous injection over 5 minutes, followed by continuous intravenous infusion at a dose of 200 micrograms/kg per hour. The dosage should be adjusted according to response, within the range of 50 to 200 micrograms/kg per hour.

◊ General references.

1. Markham A, *et al.* Nicorandil: an updated review of its use in ischaemic heart disease with emphasis on its cardioprotective effects. *Drugs* 2000; **60:** 955–74.
2. Gomma AH, *et al.* Potassium channel openers in myocardial ischaemia: therapeutic potential of nicorandil. *Drugs* 2001; **12:** 1705–10.
3. Anonymous. Nicorandil for angina – an update. *Drug Ther Bull* 2003; **41:** 86–8.
4. Simpson D, Wellington K. Nicorandil: a review of its use in the management of stable angina pectoris, including high-risk patients. *Drugs* 2004; **64:** 1941–55.

Ischaemic heart disease. A large multicentre double-blind randomised placebo-controlled study[1] suggested that nicorandil, in addition to its anti-anginal effects, may have cardioprotective properties. The incidence of major coronary events, particularly unplanned admission for chest pain, was significantly reduced in patients with stable angina at high risk of future adverse events. Nicorandil may mimic the mechanism of ischaemic pre-conditioning, whereby a brief period of ischaemia makes the myocardium resistant to damage from a further episode,[2] but it is not clear how much this mechanism contributes to its effects. There is some evidence[3-7] that nicorandil improves outcomes when given at the time of percutaneous coronary intervention, although a large study[8] in patients with myocardial infarction failed to confirm a benefit. It has been suggested[5] that an antoxidant effect may be part of the mechanism involved.

1. The IONA Study Group. Effect of nicorandil on coronary events in patients with stable angina: the Impact Of Nicorandil in Angina (IONA) randomised trial. *Lancet* 2002; **359:** 1269–75. Correction. *ibid.*; **360:** 806.
2. Lesnefsky EJ. The IONA study: preparing the myocardium for ischaemia? *Lancet* 2002; **359:** 1262–3.
3. Matsuo H, *et al.* Evidence of pharmacologic preconditioning during PTCA by intravenous pretreatment with ATP-sensitive K+ channel opener nicorandil. *Eur Heart J* 2003; **24:** 1296–1303.
4. Ikeda N, *et al.* Nicorandil versus isosorbide dinitrate as adjunctive treatment to direct balloon angioplasty in acute myocardial infarction. *Heart* 2004; **90:** 181–5.
5. Ono H, *et al.* Nicorandil improves cardiac function and clinical outcome in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention: role of inhibitory effect on reactive oxygen species formation. *Am Heart J* 2004; **148:** E15.
6. Ishii H, *et al.* Impact of a single intravenous administration of nicorandil before reperfusion in patients with ST-segment-elevation myocardial infarction. *Circulation* 2005; **112:** 1284–8.
7. Ishii H, *et al.* Effects of intravenous nicorandil before reperfusion for acute myocardial infarction in patients with stress hyperglycemia. *Diabetes Care* 2006; **29:** 202–6.
8. Kitakaze M, *et al.* J-WIND investigators. Human atrial natriuretic peptide and nicorandil as adjuncts to reperfusion treatment for acute myocardial infarction (J-WIND): two randomised trials. *Lancet* 2007; **370:** 1483–93.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Ikorel; ***Austria:*** Dancor; ***Denm.:*** Angicor; ***Fr.:*** Adancor; Ikorel; ***India:*** Corflo; Zynicor; ***Irl.:*** Ikorel; ***Ital.:*** Andilex†; ***Jpn:*** Sigmart; ***Neth.:*** Dancor; Ikorel; ***NZ:*** Ikorel; ***Port.:*** Dancor; Nikoril; ***Spain:*** Dancor; ***Switz.:*** Dancor; ***UK:*** Ikorel.

Nicotinyl Alcohol *(BAN, USAN)*

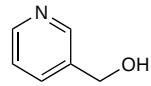
3-Hydroxymethylpyridine; Nicotinic Alcohol; Nicotinílico, alcohol; NSC-526046; NU-2121; 3-Pyridinemethanol; β-Pyridylcarbinol; Ro-1-5155. 3-Pyridylmethanol.

C_6H_7NO = 109.1.

CAS — 100-55-0.

ATC — C04AC02; C10AD05.

ATC Vet — QC04AC02; QC10AD05.



Nicotinyl Alcohol Tartrate *(BANM)*

Alcohol nicotinílico, tartrato de; Nicotinyl Tartrate. 3-Pyridylmethanol hydrogen (2*R*,3*R*)-tartrate.

$C_6H_7NO,C_4H_6O_6$ = 259.2.

CAS — 6164-87-0.

ATC — C04AC02; C10AD05.

ATC Vet — QC04AC02; QC10AD05.

Pharmacopoeias. In *Br.*

BP 2008 (Nicotinyl Alcohol Tartrate). A white or almost white, odourless or almost odourless, crystalline powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in chloroform and in ether. A 5% solution in water has a pH of 2.8 to 3.7.

Profile

Nicotinyl alcohol is a vasodilator and lipid regulating drug with general properties similar to those of nicotinic acid (p.1957), to which it is partly hydrolysed.

Nicotinyl alcohol has been given orally, as the tartrate, in the management of peripheral vascular disease, and has also been used in Ménière's disease and in hyperlipidaemias.

Preparations

BP 2008: Nicotinyl Alcohol Tablets.

Proprietary Preparations (details are given in Part 3)
Indon.: Cetacol; ***Pol.:*** Nicotol†.

Multi-ingredient: ***Braz.:*** Lipofacton.