7. Mohr JP, *et al.* Meta-analysis of oral nimodipine trials in acute ischemic stroke. *Cerebrovasc Dis* 1994; **4:** 197–203.
8. Horn J, *et al.* Very Early Nimodipine Use in Stroke (VENUS): a randomized, double-blind, placebo-controlled trial. *Stroke* 2001; **32:** 461–5.
9. Roine RO, *et al.* Nimodipine after resuscitation from out-of-hospital ventricular fibrillation: a placebo-controlled, double-blind, randomized trial. *JAMA* 1990; **264:** 3171–7.
10. Parnetti L, *et al.* Nimodipine Study Group. Mental deterioration in old age: results of two multicenter, clinical trials with nimodipine. *Clin Ther* 1993; **15:** 394–406.
11. López-Arrieta J, Birks J. Nimodipine for primary degenerative, mixed and vascular dementia. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2002 (accessed 12/07/05).

Migraine and cluster headache. For reference to the use of calcium-channel blockers, including nimodipine, in the management of migraine and cluster headache, see under Nifedipine, p.1355.

Preparations

BP 2008: Nimodipine Intravenous Infusion; Nimodipine Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: AC Vascular; Acival; Ampina; Aniduv; Cebrofort; Cletonol†; Eugerial; Explaner; Finacilen; Macobal; Nimo-Somazina; Nimodilat; Nimotop; Nivas; Tenocard; ***Austral.:*** Nimotop; ***Austria:*** Nimotop; ***Belg.:*** Nimotop; ***Braz.:*** Eugerial; Neuron; Nimobal; Nimopax; Nimotop; Nimovas†; Noodipina; Norton†; Oxigen; Vasodipina; ***Canad.:*** Nimotop; ***Chile:*** Brainal†; Grifonimod; Neurogeron†; Nimotop; Regental; Vasoflex†; ***Cz.:*** Brainal†; Dilceren; Nimotop; ***Denm.:*** Nimotop; ***Fin.:*** Nimotop; ***Fr.:*** Nimotop; ***Ger.:*** Nim†; Nimotop; ***Gr.:*** Aurodipine; Befimat; Curban; Figozant; Genovox; Myodipine; Naborel; Nelbinex†; Nimodil; Nimotop; Nimovac-V; Nortolan; Rosital; Stigmicarpin; Thrionipen; Vastripine; Ziremex; ***Hong Kong:*** Nimotop; ***Hung.:*** Nimotop; ***India:*** Vasotop; ***Indon.:*** Nimotop; ***Irl.:*** Nimotop; ***Israel:*** Nimotop; ***Ital.:*** Nimotop; Periplum; ***Malaysia:*** Nimotop†; ***Mex.:*** Kenzolol; Nimotop; Vacer; ***Neth.:*** Nimotop; ***Norw.:*** Nimotop; ***NZ:*** Nimotop; ***Philipp.:*** Nimotop; ***Pol.:*** Nimotop; ***Port.:*** Brainox; Genogris; Modibloq; Modina; Nimotop; Sobrepina; Trinalion; ***Rus.:*** Brainal (Брейнал)†; Nemotan (Немотан); Nimotop (Нимотоп); ***S.Afr.:*** Nimotop; ***Singapore:*** Nimotop; ***Spain:*** Admon; Brainal; Calnit; Kenesil; Modus; Nimotop; Remontal; ***Swed.:*** Nimotop; ***Switz.:*** Nimotop; ***Thai.:*** Nimotop; ***Turk.:*** Nimotop; ***UK:*** Nimotop; ***USA:*** Nimotop; ***Venez.:*** Kleren†; Nemodine; Nimotop; Tropocer.

Multi-ingredient: ***Arg.:*** Idesole Plus; Nemocebral Plus; Nimodilat Plus; Nimoreagin; Nivas Plus.

Nisoldipine *(BAN, USAN, rINN)*

Bay-k-5552; Nisoldipiini; Nisoldipin; Nisoldipino; Nisoldipinum. Isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate.

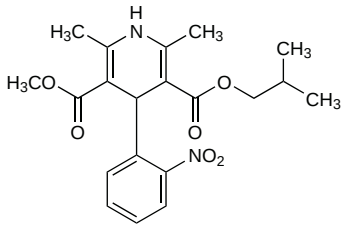
Низольдипин

$C_{20}H_{24}N_2O_6$ = 388.4.

CAS — 63675-72-9.

ATC — C08CA07.

ATC Vet — QC08CA07.



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

Nisoldipine is well absorbed from the gastrointestinal tract after oral doses but undergoes rapid and extensive first-pass metabolism in the gut wall and liver and bioavailability has been reported to be only about 4 to 8%. About 60 to 80% of an oral dose is excreted in the urine and the remainder in the faeces, mainly as metabolites. The terminal elimination half-life is about 7 to 12 hours. Nisoldipine is more than 99% bound to plasma proteins.

◊ A study[1] in 11 patients given oral nisoldipine 10 mg once or twice daily indicated that the pharmacokinetics of nisoldipine could best be described by an open 2-compartment model. Peak plasma concentrations occurred 1 hour after a single oral dose, and varied greatly between the patients. The mean plasma elimination half-life was 11.4 hours after a single dose and 14.0 hours after repeated dosing, which was longer than had been previously reported, perhaps reflecting the greater sensitivity of the assay.

In another study oral, but not intravenous, nisoldipine increased liver blood flow in 10 healthy subjects and thus affected its own systemic availability.[2] Variations in liver blood flow may account for the interindividual variation in the pharmacokinetics of nisoldipine.

1. Ottosson A-M, *et al.* Analysis and pharmacokinetics of nisoldipine in hypertensive patients. *Curr Ther Res* 1989; **45:** 347–58.
2. van Harten J, *et al.* Variability in the pharmacokinetics of nisoldipine as caused by differences in liver blood flow response. *J Clin Pharmacol* 1989; **29:** 714–21.

Uses and Administration

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

Nisoldipine is given orally usually as a modified-release preparation. Absorption is affected by food and the modified-release preparation should be taken on an empty stomach; it should not be taken with high fat meals. Doses are similar for both hypertension and angina. The initial dose is 10 mg once daily and the usual maintenance dose is 20 to 40 mg once daily.

◊ Reviews.

1. Mitchell J, *et al.* Nisoldipine: a new dihydropyridine calcium-channel blocker. *J Clin Pharmacol* 1993; **33:** 46–52.
2. Plosker GL, Faulds D. Nisoldipine coat-core: a review of its pharmacology and therapeutic efficacy in hypertension. *Drugs* 1996; **52:** 232–53.
3. Langtry HD, Spencer CM. Nisoldipine coat-core; a review of its pharmacodynamic and pharmacokinetic properties and clinical efficacy in the management of ischaemic heart disease. *Drugs* 1997; **53:** 867–84.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Nisodipen†; ***Austria:*** Syscor; ***Belg.:*** Sular; Syscor; ***Braz.:*** Syscor; ***Chile:*** Nivas; ***Cz.:*** Syscor†; ***Fin.:*** Syscor; ***Ger.:*** Baymycard; ***Gr.:*** Syscor; ***Hung.:*** Baymycard; ***Ital.:*** Syscor; ***NZ:*** Syscor; ***S.Afr.:*** Syscor†; ***Spain:*** Cornel†; Sular; Syscor; ***Switz.:*** Syscor†; ***UK:*** Syscor; ***USA:*** Sular.

Nitrendipine *(BAN, USAN, rINN)*

Bay-e-5009; Nitrendipiini; Nitrendipin; Nitrendipinas; Nitrendipino; Nitrendipinum. Ethyl methyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate.

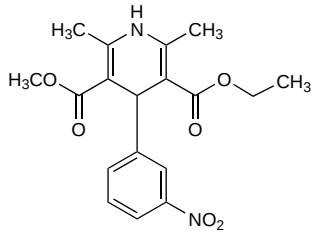
Нитрендипин

$C_{18}H_{20}N_2O_6$ = 360.4.

CAS — 39562-70-4.

ATC — C08CA08.

ATC Vet — QC08CA08.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn*.
Ph. Eur. 6.2 (Nitrendipine). A yellow crystalline powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in dehydrated alcohol and in methyl alcohol; freely soluble in ethyl acetate. Exposure to ultraviolet light leads to formation of a nitrophenylpyridine derivative. Solutions should be prepared in the dark or under light of wavelength greater than 420 nm, immediately before use. Protect from light.

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

Nitrendipine is reported to be well absorbed after oral doses but undergoes extensive first-pass metabolism; the absolute oral bioavailability is reported to range from about 10 to 20%, depending in part on the dosage form. Nitrendipine is about 98% bound to plasma proteins. It is extensively metabolised in the liver and is excreted as metabolites, mainly in urine, with small amounts in the faeces. Although early studies reported a terminal elimination half-life of about 2 to 4 hours, later studies, using more sensitive assay procedures, have recorded values between about 10 and 22 hours.

◊ References.

1. Soons PA, Breimer DD. Stereoselective pharmacokinetics of oral and intravenous nitrendipine in healthy male subjects. *Br J Clin Pharmacol* 1991; **32:** 11–16.

Uses and Administration

Nitrendipine is a dihydropyridine calcium-channel blocker with actions similar to those of nifedipine (p.1354). It is used in the treatment of hypertension (p.1171).

The usual dose is 20 mg daily as a single oral dose or as 2 divided doses. The dose may be increased to 20 mg twice daily if necessary for the control of resistant hypertension. In the elderly, an initial dose of 10 mg daily should be used. The dose should also be reduced in hepatic impairment (see below).

◊ Reviews.

1. Santiago TM, Lopez LM. Nitrendipine: a new dihydropyridine calcium-channel antagonist for the treatment of hypertension. *DICP Ann Pharmacother* 1990; **24:** 167–75.

Administration in hepatic impairment. The initial dose of nitrendipine should be reduced to 5 to 10 mg once daily in patients with hepatic impairment.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Nirapel; Nitrendil; Tocrat†; ***Austria:*** Baypress; ***Belg.:*** Baypress; ***Braz.:*** Caltren; Nitrencord; ***Chile:*** Cardiazem; Grifonitren; Nitrendicor†; Presabet†; Tensofar; ***Cz.:*** Baypress; Lusopress; Nitrepress; Nitresan; Unipres; ***Denm.:*** Baypress; ***Fr.:*** Baypress; Nidrel; ***Ger.:*** Bayotensin; Jutapress; Nitre; Nitre-Puren; Nitregamma; Nitren Lich; Nitren†; Nitrendepat†; Nitrendidoc; Nitrendimerck†; Nitrensal; Nitrepress; ***Gr.:*** Aroselin; Baypress; Crivion; G-Press; Lanocardique†; Leonitren; Lisba; Lostradyl; Midonat†; Nelconil; Nifecard; Nivitron; Pallohyman†; Potional; Pressodipin; Spidox; Tepanil†; Ufocard; ***Hong Kong:*** Baypress; ***Hung.:*** Baypress; Unipres; ***Ital.:*** Baypress; Deiten; ***Jpn:*** Baylotensin; ***Mex.:*** Baypress†; ***Neth.:*** Baypress; ***Port.:*** Baypress; Farnitran; Hiperdipina; Hipertenol†; ***Spain:*** Balminil†; Baypresol; Gericin; Niprina; Sub Tensin; Tensogradal; Trendinol†; Vastensium; ***Switz.:*** Baypress; ***Thai.:*** Baypress; Ditrenil; Miniten; ***Turk.:*** Baypress; ***Venez.:*** Baypress; Nitrendil; Retencal†.

Multi-ingredient: ***Ger.:*** Eneas; ***Gr.:*** Eneas; Enit; ***India:*** Cardif Beta; ***Port.:*** Eneas; Enit; ***Spain:*** Eneas; Enit; Vipres; Zorail.

Nitric Oxide *(USAN)*

Azote, monoxyde d'; Azoto oksidas; Azotu(II) tlenek; Kväveoxid; Mononitrogen Monoxide; Nitrogen Monoxide; Nitrogenii oxidum; Nitrogén-monoxid; OHM-11771; Oxid dusnatý; Óxido nítrico; Typpioksidi.

NO = 30.01.

CAS — 10102-43-9.

ATC — R07AX01.

ATC Vet — QR07AX01.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Nitric Oxide). A colourless gas that turns brown when exposed to air. At 20° and at a pressure of 101 kPa, 1 volume dissolves in about 21 volumes of water. Store compressed at a pressure not exceeding 2.5 MPa measured at 15° in suitable containers.

Adverse Effects

Inhaled nitric oxide may lead to the development of methaemoglobinaemia, particularly at higher doses. Although it is a selective pulmonary vasodilator, systemic hypotension may occur. Abrupt withdrawal of therapy may lead to a deterioration in oxygenation and the development of rebound pulmonary hypertension.

Nitrogen dioxide produced when nitric oxide combines with oxygen can cause acute lung injury; high concentrations of inhaled nitric oxide are directly irritant to the lungs.

◊ A potential complication of inhaled nitric oxide is methaemoglobinaemia but this is probably related to the dose; the risk does not appear to be increased during low-dose (20 ppm) therapy.[1] Another possible adverse event is an increased risk of bleeding due to inhibition of platelet aggregation.[2-5] Rebound pulmonary hypertension[6] and deterioration in oxygenation[7,8] have been reported in some children after stopping nitric oxide therapy. Severe systemic hypotension has also been reported[9] after starting therapy in a neonate with severe left ventricular dysfunction. Pulmonary oedema has been associated with the use of nitric oxide in 2 patients with CREST syndrome, a form of systemic sclerosis.[10] Motor neurone disease in a patient with alcoholism has been partly attributed[11] to the use of nitric oxide for pulmonary hypertension.

1. Kinsella JP, Abman SH. Methaemoglobin during nitric oxide therapy with high-frequency ventilation. *Lancet* 1993; **342:** 615.