

Fedipisal†; Atenses; Cordilat; Corogal; Corotrend; Fusepina; Gelprim; Nifedigel; Nifedipres; Nifetzard; Nifiser; Noviken; **Neth.**: Adalat; **Norw.**: Adalat; **NZ.**: Adalat; **Adefin.**: Nyefax; **Philipp.**: Adalat; Calcheck; Calcibloc; Calcigard; Cardiac; Darat; Heblopin; Nelapine; Nifestad; Normadil; Odipin; Temsibloc; **Pol.**: Adalat; Cordafen; **Port.**: Adalat; Angipina; Meborilan; Medipina†; Nifedat†; Zenusin; **Rus.**: Adalat (Адалат); Calcigard (Кальцигард); Cordafen (Кордафен); Cordaflex (Кордафлекс); Cordipin (Кордипин); Corinfar (Коринфар); Depin-E (Депин-Е); Fenamon (Фенамон); Nicardia (Никардия); Nifecard (Нифекард); Osmo-Adalat (Осмо-Адалат); **S.Afr.**: Adalat; Cardifen; Cardilat†; Cipalat; Nifedalat; Vascard; **Singapore.**: Adalat; Apo-Nifedil; Calcigard; Cordipin; Fenamon; Nifecard†; Nifedi-Denk†; Nifelat†; Nipin; Stada Uno; Vasdalat†; **Spain.**: Adalat; Dilcor; Pertensal; **Swed.**: Adalat; **Switz.**: Adalat; Aldipin†; Cardipin; Corotrend; Ecodipine; nife-basan†; Nifedilcor; **Thai.**: Adalat; Calcigard; Coracten; Fenamon; Nelapine; Nifecard; Nifelat; Nifiran†; Nyefax; Stada Uno; **Turk.**: Adalat; Kardilat; Nidicard; Nidilat; **UAE.**: Cardiopine; **UK.**: Adalat; Adipine; Angiopine†; Calchan; Cardilate MR; Coracten; Coroday†; Fortipine; Hypolar Retard; Nifedipres; Nifopress; Slofedipine; Tensipine; **USA.**: Adalat; Afeditab; Nifedical; Nifedical; Procardia; **Venez.**: Adalat; Conducl; Fedilex†; Nifal; Tensomax; Tensopin.

**Multi-ingredient:** **Arg.**: Atel N†; **Austria:** Beta-Adalat; Nif-Ten; Pontuc; **Belg.**: Beta-Adalat†; Tenif; **Braz.**: Nifelat; **Fin.**: Nif-Ten; **Fr.**: Beta-Adalat; Tenordate; **Ger.**: AteNif beta; Belnif; Bresben; duranifin Sali†; Nif-Ten; Nifatenol; Sali-Adalat; Tredalat; **Hong Kong:** Nif-Ten; **India:** Beta Nicardia†; Cardules Plus; Depten; Nifetolol; Presolar; Tenofed; **Indon.**: Nif-Ten; **Irl.**: Beta-Adalat; Nif-Ten; **Ital.**: Antrolin; Mixer; Nif-Ten; **Mex.**: Plenacor; **Neth.**: Nif-Ten†; **Philipp.**: Nif-Ten; **Singapore:** Beta Nicardia; Nif-Ten; Nifetex; **Switz.**: Beta-Adalat; Nif-Atenil; Nif-Ten; **UK:** Beta-Adalat; Tenif.

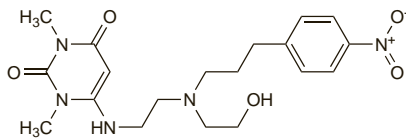
### Nifekalant Hydrochloride (rINN)

Hydrochloruro de nifekalant; MS-55 I; Nifekalant, Chlorhydrate de; Nifekalanti Hydrochloridum. 6-[[2-((2-Hydroxyethyl)[3-(p-nitrophenyl)propyl]amino)ethyl]amino]-1,3-dimethyluracl hydrochloride.

Нифекаланта Гидрохлорид

C<sub>19</sub>H<sub>27</sub>N<sub>5</sub>O<sub>5</sub>·HCl = 441.9.

CAS — 130636-43-0 (nifekalant); 130656-51-8 (nifekalant hydrochloride).



(nifekalant)

### Profile

Nifekalant is a class III antiarrhythmic (p.1153) used intravenously as the hydrochloride in the management of life-threatening ventricular arrhythmias (p.1160).

### References

- Katoh T, *et al.* Emergency treatment with nifekalant, a novel class III anti-arrhythmic agent, for life-threatening refractory ventricular tachyarrhythmias: post-marketing special investigation. *Circ J* 2005; **69**: 1237–43.

**Effects on the heart.** A woman who had been receiving intravenous nifekalant continuously for 10 months was found<sup>1</sup> to have a round mass in the right atrium. This was resected and shown to be a fibrin thrombus containing a large amount of nifekalant in the form of needle crystals.

- Okamura H, *et al.* Crystals in the heart. *Heart* 2004; **90**: 1106.

### Preparations

**Proprietary Preparations** (details are given in Part 3)

**Jpn:** Shinbit.

### Nilvadipine (USAN, rINN)

CL-287389; FK-235; Nilvadipiidiin; Nilvadipidin; Nilvadipidinum; Nilvadipino; Nilvadipinum; Nivadipine; SKF-102362. 5-Isopropyl 3-methyl 2-cyano-1,4-dihydro-6-methyl-4-(*m*-nitrophenyl)-3,5-pyridinedicarboxylate.

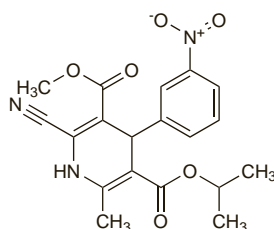
Нильвадипин

C<sub>19</sub>H<sub>19</sub>N<sub>3</sub>O<sub>6</sub> = 385.4.

CAS — 75530-68-6.

ATC — C08CA10.

ATC Vet — QC08CA10.



The symbol † denotes a preparation no longer actively marketed

### Pharmacopoeias. In *Jpn.*

### Profile

Nilvadipine is a dihydropyridine calcium-channel blocker with general properties similar to those of nifedipine (p.1350). It is used in the management of hypertension (p.1171). Nilvadipine is given orally, usually as a modified-release preparation, in a dose of up to 16 mg daily.

### Reviews

- Brogden RN, McTavish D. Nilvadipine: a review of its pharmacodynamic and pharmacokinetic properties, therapeutic use in hypertension and potential in cerebrovascular disease and angina. *Drugs Aging* 1995; **6**: 150–71. Correction. *ibid.*; **7**: 116.

### Preparations

**Proprietary Preparations** (details are given in Part 3)

**Austria:** Tensan; **Cz.**: Escor; **Fin.**: Escor; **Ger.**: Escor; Nivadil; **Gr.**: Peroma; **Irl.**: Nivadil; **Jpn:** Nivadil; **Port.**: Nivadil; **Switz.**: Nivadil†; **Turk.**: Nilvadis.

### Nimodipine (BAN, USAN, rINN)

Bay-e-9736; Nimodipiini; Nimodipin; Nimodipinas; Nimodipino; Nimodipinum; Nimodypina. Isopropyl 2-methoxyethyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate.

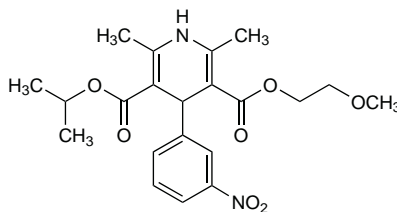
Нимодипин

C<sub>21</sub>H<sub>26</sub>N<sub>2</sub>O<sub>7</sub> = 418.4.

CAS — 66085-59-4.

ATC — C08CA06.

ATC Vet — QC08CA06.



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

**Ph. Eur. 6.2** (Nimodipine). A light yellow or yellow crystalline powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in dehydrated 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.

**USP 31** (Nimodipine). A light yellow or yellow crystalline powder, affected by light. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in ethyl acetate. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

**Incompatibility.** Licensed product information states that solutions of nimodipine are incompatible with some plastics, including PVC, and that the only plastics suitable for use are polyethylene and polypropylene.

### Adverse Effects, Treatment, and Precautions

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

Nimodipine should be used with caution in patients with cerebral oedema or severely raised intracranial pressure.

**Effects on the heart.** Marked bradycardia developed in a patient with acute ischaemic stroke during treatment with nimodipine and was suspected to be related to the drug therapy.<sup>1</sup>

- Fagan SC, Nacci N. Nimodipine and bradycardia in acute stroke—drug or disease? *DICP Ann Pharmacother* 1991; **25**: 247–9.

### Interactions

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

### Pharmacokinetics

Nimodipine is rapidly absorbed from the gastrointestinal tract after oral doses but undergoes extensive first-pass metabolism in the liver. The oral bioavailability is reported to be about 13%. Nimodipine is more than 95% bound to plasma proteins. It crosses the blood-brain barrier, but concentrations in CSF are lower than those in plasma. Nimodipine is extensively metabolised in the liver. It is excreted in faeces via the bile, and in urine, almost entirely as metabolites. The terminal

elimination half-life is reported to be about 9 hours but the initial decline in plasma concentration is much more rapid, equivalent to a half-life of 1 to 2 hours.

### Uses and Administration

Nimodipine is a dihydropyridine calcium-channel blocker that has the general properties of nifedipine (p.1354), but acts particularly on cerebral blood vessels. It is used in cerebrovascular disorders (see below), particularly in the prevention and treatment of ischaemic neurological deficits after aneurysmal subarachnoid haemorrhage.

To reduce the incidence and severity of neurological deficit after aneurysmal haemorrhage nimodipine is given orally in a dose of 60 mg every 4 hours. Treatment should begin within 4 days of onset of haemorrhage and should continue for 21 days. In patients with hepatic impairment the dose may be reduced (see below) and blood pressure should be closely monitored.

If cerebral ischaemia occurs or has already occurred, neurological deficit may be treated by intravenous infusion of nimodipine. It should be given via a bypass into a running intravenous infusion into a central vein. The initial dose should be nimodipine 1 mg/hour for 2 hours, increased (provided that no severe decrease in blood pressure occurs) to 2 mg/hour. The starting dose should be reduced to 500 micrograms/hour, or even lower if necessary, in patients weighing less than 70 kg and in those with unstable blood pressure; a similar reduction in dosage has been suggested in hepatic impairment, and blood pressure should be closely monitored. Treatment should be started as soon as possible and continued for at least 5 and no more than 14 days; if the patient has already received oral nimodipine, the total duration of nimodipine use should not exceed 21 days.

**Administration in hepatic impairment.** The clearance of nimodipine is reduced in patients with cirrhosis, and blood pressure should be closely monitored in such patients. US licensed product information recommends that the oral dose of nimodipine should be halved to 30 mg every 4 hours in patients with hepatic cirrhosis. Some manufacturers have also suggested a reduction in the initial intravenous dose to 500 micrograms or less per hour.

**Cerebrovascular disorders.** Nimodipine is used orally and intravenously in the prevention and treatment of ischaemic neurological deficits caused by arterial vasospasm after aneurysmal subarachnoid haemorrhage (see Stroke, p.1185), although the evidence for benefit after intravenous use is limited.<sup>1</sup> Nimodipine has also been used for traumatic subarachnoid haemorrhage,<sup>2</sup> but results have been mixed.<sup>3,4</sup> In addition to dilating cerebral blood vessels and improving cerebral blood flow, nimodipine may also prevent or reverse ischaemic damage to the brain by limiting transcellular calcium influx.

These effects have led to the investigation of nimodipine in other conditions associated with cerebral ischaemia. Studies<sup>5,6</sup> of nimodipine given orally after ischaemic stroke have produced conflicting results. A meta-analysis<sup>7</sup> of controlled studies suggested that nimodipine is beneficial if given within 12 hours of stroke onset but a further study<sup>8</sup> failed to confirm these findings. In a controlled study<sup>9</sup> of 155 patients suffering a cardiac arrest, nimodipine was given by intravenous infusion for 24 hours. Nimodipine had no effect on overall survival, although it did improve survival of patients in whom advanced life support was delayed for more than 10 minutes after arrest. Nimodipine has also been tried in dementia (p.362). Two multicentre studies<sup>10</sup> involving a total of 755 patients with dementia of vascular or degenerative origin given nimodipine for up to 6 months reported improvements in cognitive function and disability, and a systematic review<sup>11</sup> concluded that nimodipine could be of some benefit in patients with various forms of dementia.

- 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 12/03/08).
- Harders A, *et al.* Traumatic subarachnoid hemorrhage and its treatment with nimodipine. *J Neurosurg* 1996; **85**: 82–9.
- Langham J, *et al.* Calcium channel blockers for acute traumatic brain injury. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2003 (accessed 12/03/08).
- Vergouwen MDI, *et al.* Effect of nimodipine on outcome in patients with traumatic subarachnoid haemorrhage: a systematic review. *Lancet Neurol* 2006; **5**: 1029–32.
- Gelmers HJ, *et al.* A controlled trial of nimodipine in acute ischaemic stroke. *N Engl J Med* 1988; **318**: 203–7.
- Trust Study Group. Randomised, double-blind, placebo-controlled trial of nimodipine in acute stroke. *Lancet* 1990; **336**: 1205–9.

- Mohr JP, et al. Meta-analysis of oral nimodipine trials in acute ischemic stroke. *Cerebrovasc Dis* 1994; **4**: 197–203.
- Horn J, et al. Very Early Nimodipine Use in Stroke (VENUS): a randomized, double-blind, placebo-controlled trial. *Stroke* 2001; **32**: 461–5.
- 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.
- Pametti 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.
- 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; Finaclen; Macobal; Nimo-Somazina; Nimodilat; Nimotop; Nivas; Tenocard; **Austral.:** Nimotop; **Austria:** Nimotop; **Belg.:** Nimotop; **Braz.:** Eugerial; Neuron; Nimbol; Nimopax; Nimotop; Nimovas; Noodipina; Norton; Oxigen; Vasodipina; **Canad.:** Nimotop; **Chile:** Brainal; Grifonimod; Neurogeron; Nimotop; Regental; Vasoflex; **Cz.:** Brainal; Dileren; Nimotop; **Denm.:** Nimotop; **Fin.:** Nimotop; **Fr.:** Nimotop; **Ger.:** Nim; Nimotop; **Gr.:** Aurodipine; Befimat; Curban; Figozant; Genovox; Myodipine; Naborel; Nelbine; Nimodil; Nimodil; Nimovac-V; Nortolan; Rosital; Stignicaripin; Thronipen; Vastripine; Ziremex; **Hong Kong:** Nimotop; **Hung.:** Nimotop; **India:** Vasotop; **Indon.:** Nimotop; **Isl.:** 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; Modiblo; Modina; Nimotop; Sobrepina; Tinalion; **Rus.:** Brainal (Бреинал); Nemo-tan (Немостан); Nimotop (Нимотоп); **S.Afr.:** Nimotop; **Singapore:** Nimotop; **Spain:** Admon; Brainal; Calnit; Kenesi; Modus; Nimotop; Remontal; **Swed.:** Nimotop; **Switz.:** Nimotop; **Thai.:** Nimotop; **Turk.:** Nimotop; **UK:** Nimotop; **USA:** Nimotop; **Venez.:** Klerent; 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.

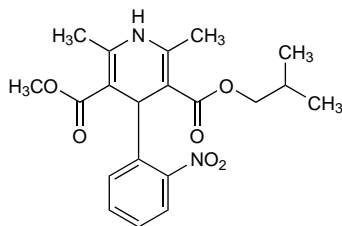
Низольдипин

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

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<sup>1</sup> 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.<sup>2</sup> Variations in liver blood flow may account for the interindividual variation in the pharmacokinetics of nisoldipine.

- Ottosson A-M, et al. Analysis and pharmacokinetics of nisoldipine in hypertensive patients. *Curr Ther Res* 1989; **45**: 347–58.
- 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.

- Mitchell J, et al. Nisoldipine: a new dihydropyridine calcium-channel blocker. *J Clin Pharmacol* 1993; **33**: 46–52.
- Plosker GL, Faulds D. Nisoldipine coat-core: a review of its pharmacology and therapeutic efficacy in hypertension. *Drugs* 1996; **52**: 232–53.
- 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.:** Nisoldipent; **Austria:** Sycor; **Belg.:** Sular; Sycor; **Braz.:** Sycor; **Chile:** Nivas; **Cz.:** Sycor; **Fin.:** Sycor; **Ger.:** Baymycard; **Gr.:** Sycor; **Hung.:** Baymycard; **Ital.:** Sycor; **NZ:** Sycor; **S.Afr.:** Sycor; **Spain:** Cornel; Sular; Sycor; **Switz.:** Sycor; **UK:** Sycor; **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.

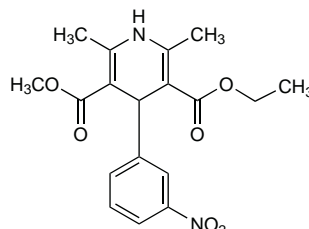
Нитрендипин

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

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.

- 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.

- Santiago TM, Lopez LM. Nitrendipine: a new dihydropyridine calcium-channel antagonist for the treatment of hypertension. *Drugs* 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; Nitrendicord; **Chile:** Cardiazem; Grifonitren; Nitrendicord; Presabet; Tensofar; **Cz.:** Baypress; Lusopress; Nitrepres; Nitresan; Unipres; **Denm.:** Baypress; **Fr.:** Baypress; Nidret; **Ger.:** Bayotensin; Jutapress; Nitre; Nitre-Puren; Nitregamma; Nitren Licht; Nitren; Nitrendepat; Nitrendidoc; Nitrendimerck; Nitrensil; Nitrepres; **Gr.:** Aroselin; Baypress; Crivion; G-Press; Lanocardique; Leonitren; Lisa; Lostradyl; Midonat; Nelconil; Nifecard; Nitvtron; Pallohyman; Potional; Pressodipin; Spidox; Tepanil; Ufo-card; **Hong Kong:** Baypress; **Hung.:** Baypress; Unipres; **Ital.:** Baypress; Deter; **Jpn.:** Baylotensin; **Mex.:** Baypress; **Neth.:** Baypress; **Port.:** Baypress; Farnitran; Hiperdipina; Hipertenol; **Spain:** Balmilil; Baypresol; Genic; Niprina; Sub Tensin; Tensogradal; Trendinol; Vastensium; **Switz.:** Baypress; **Thai.:** Baypress; Ditretil; 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; Nitrogen-monoxid; OHM-11771; Oxid dusnaty; Oxido nítrico; Typpioksid.

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.<sup>1</sup> Another possible adverse event is an increased risk of bleeding due to inhibition of platelet aggregation.<sup>2-5</sup> Rebound pulmonary hypertension<sup>6</sup> and deterioration in oxygenation<sup>7,8</sup> have been reported in some children after stopping nitric oxide therapy. Severe systemic hypotension has also been reported<sup>9</sup> 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.<sup>10</sup> Motor neurone disease in a patient with alcoholism has been partly attributed<sup>11</sup> to the use of nitric oxide for pulmonary hypertension.

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