Fedipisal†; Atenses; Cordilat; Corogal; Corotrend; Fusepina; Gelprim; Nifedigel; Nifedipres; Nifezzard; Nifser; Noviken; **Neth.:** Adalat; **Norw.:** Adalat; **NZ:** Adalat; Adefin; Nyefax; **Philipp.:** Adalat; Calcheck; Calcibloc; Calcigard; Cardicap; Darat; Heblopin; Nelapine; Nifestad; Normadil; Odipin; Tensibloc; **Pol.:** Adalat; Cordafen; Cordipin; **Port.:** Adalat; Angipina; Meborilan; Medipina†; Nifedate†; 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-Nifed; 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†; Nifedicor; **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; Corodaγ†; Fortipine; Hypolar Retard; Nifedipress; Nifopress; Slofedipine; Tensipine; **USA:** Adalat; Afeditab; Nifediac; Nifedical; Procardia; **Venez.:** Adalat; Conducil; 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-Adalate; 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.

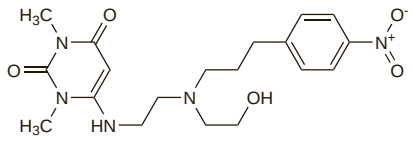
Nifekalant Hydrochloride *(rINNM)*

Hidrocloruro de nifekalant; MS-551; Nifékalant, Chlorhydrate de; Nifekalanti Hydrochloridum. 6-[(2-{(2-Hydroxyethyl)[3-(*p*-nitrophenyl)propyl]amino}ethyl)amino]-1,3-dimethyluracil hydrochloride.

Нифекаланта Гидрохлорид

$C_{19}H_{27}N_5O_5,HCl$ = 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.

1. 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[1] 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.

1. 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; Nilvadipidiini; Nilvadipidin; Nilvadipidinum; Nilvadipin; Nilvadipino; Nilvadipinum; Nivadipine; SKF-102362. 5-Isopropyl 3-methyl 2-cyano-1,4-dihydro-6-methyl-4-(*m*-nitrophenyl)-3,5-pyridinedicarboxylate.

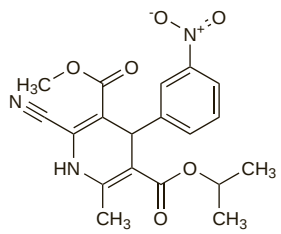
Нильвадипин

$C_{19}H_{19}N_3O_6$ = 385.4.

CAS — 75530-68-6.

ATC — C08CA10.

ATC Vet — QC08CA10.



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.

1. 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.

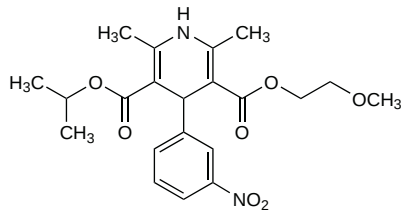
Нимодипин

$C_{21}H_{26}N_2O_7$ = 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.[1]

1. 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.[1] Nimodipine has also been used for traumatic subarachnoid haemorrhage,[2] but results have been mixed.[3,4] 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[5,6] of nimodipine given orally after ischaemic stroke have produced conflicting results. A meta-analysis[7] of controlled studies suggested that nimodipine is beneficial if given within 12 hours of stroke onset but a further study[8] failed to confirm these findings. In a controlled study[9] 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[10] 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[11] concluded that nimodipine could be of some benefit in patients with various forms of dementia.

1. 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).
2. Harders A, *et al.* Traumatic subarachnoid hemorrhage and its treatment with nimodipine. *J Neurosurg* 1996; **85:** 82–9.
3. 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).
4. Vergouwen MDI, *et al.* Effect of nimodipine on outcome in patients with traumatic subarachnoid haemorrhage: a systematic review. *Lancet Neurol* 2006; **5:** 1029–32.
5. Gelmers HJ, *et al.* A controlled trial of nimodipine in acute ischemic stroke. *N Engl J Med* 1988; **318:** 203–7.
6. Trust Study Group. Randomised, double-blind, placebo-controlled trial of nimodipine in acute stroke. *Lancet* 1990; **336:** 1205–9.