1. Name of the medicinal product

NIMOTOP 30 mg coated tablets
NIMOTOP 30 mg effervescent granules
NIMOTOP 30 mg/0.75 ml oral drops, solution

2. Qualitative and quantitative composition

NIMOTOP 30 mg coated tablets
Each coated tablet contains:
active substance: nimodipine 30 mg

NIMOTOP 30 mg/0.75 ml oral drops, solution
0.75 ml of solution contain:
active substance: nimodipine 30 mg

NIMOTOP 30mg effervescent granules
each sachet contains:
active substance: nimodipine 30 mg

For excipients, see paragraph 6.1

3. Pharmaceutical form

coated tablets
oral drops, solution.
effervescent granules:

4. Clinical information

4.1. Therapeutic indications

Prevention and treatment of ischaemic neurological deficits including those related to cerebral vasospasm.

4.2. Posology and method of administration

Unless otherwise prescribed, the recommended daily dose is 30 mg tid (1 tablet or 1 sachet or 0.75 ml of solution 3 times a day). 0.75 ml of solution is equal to 30 mg of nimodipine and corresponds to the dropper filled to the mark.

In patients with severely impaired kidney function (glomerular filtration rate < 20 ml/min) the need for treatment with Nimotop should be carefully considered and follow up examination should be carried out regularly.

In the presence of severe alterations in renal and hepatic function, any side effects, such as a fall in blood pressure, may be more pronounced; in these cases, if necessary, the dose should be reduced or treatment suspended.

In patients who develop adverse reactions the dose should be reduced as necessary or the treatment discontinued.

Upon co-administration with CYP 3A4 inhibitors or CYP 3A4 inducers a doseadaptation may be necessary (see paragraph 4.5 „Interactions with other medicaments and other forms of interaction“).

In the prevention and treatment of ischaemic neurological deficits consequent on cerebral vasospasm induced by subarachnoid haemorrhage, once the parenteral treatment has been completed, continuation of administration of nimodipine by the oral route for approximately seven days is recommended (60 mg – 2 x 30 mg tablets or sachets, or 1.5 ml of solution corresponding to 2 droppers full to the mark - 6 times a day, at 4-hourly intervals).

Nimotop should be taken outside of mealtimes, taking the tablets with a little liquid, the drops diluted in a small quantity of water, and the sachet by dissolving its contents in a small quantity of water.

Do not drink it with grapefruit juice (see paragraph 4.5, “Interactions with other medicinal product and other forms of interaction”).

Do not immerse the dropper in water and do not rinse it. After putting the drops in water, return the dropper to the bottle.

The interval between individual administrations should be not less than 4 hours.

4.3. Contraindications

Nimotop must not be administered to pregnant or breastfeeding women, or in cases of hypersensitivity to the active substance or to any of the excipients.

Nimotop must not be administered in concomitance with rifampicin, since the contemporaneous intake of rifampicin can significantly reduce the efficacy of the nimodipine (see paragraph 4.5, “Interactions with other medicinal products and other forms of interaction”).
Severely impaired liver function, particularly liver cirrhosis, may result in an increased bioavailability of nimodipine due to a decreased first pass capacity and a reduced metabolic clearance. Therefore, nimodipine must not be administered for treatment of ischemic neurological deficits to patients with severely impaired liver function (e.g. cirrhosis of the liver).

The concomitant use of oral nimodipine and the antiepileptic drugs phenobarbital, phenytoin or carbamazepine is contraindicated as efficacy of nimodipine could be significantly reduced (see paragraph 4.5, “Interactions with other medicinal products and other forms of interaction”).

4.4. Special warnings and precautions for use

Although treatment with nimodipine has not been shown to be associated with increases in intracranial pressure, close monitoring is recommended in these cases or when the water content of the brain tissue is elevated (generalized cerebral edema).

Caution is required in patients with severe hypotension (systolic blood pressure lower than 100 mm Hg).

In very old multimorbid patients, in case of severely impaired kidney function (glomerular filtration rate < 20 ml/min), and in those with severely impaired cardiovascular function the need for treatment with Nimotop should be carefully considered and follow-up examination should be carried out regularly.

Nimodipine is metabolized via the cytochrome P450 3A4 system. Drugs that are known to either inhibit or to induce this enzyme system may therefore alter the first pass (after oral administration) or the clearance of nimodipine (see paragraph 4.5, “Interactions with other medicinal products and other forms of interaction”).

Drugs, which are known inhibitors of the cytochrome P450 3A4 system and therefore may lead to increased plasma concentrations of nimodipine are, e.g.:
- macrolide antibiotics (e.g., erythromycin),
- anti-HIV protease inhibitors (e.g., ritonavir),
- azole antimycotics (e.g., ketoconazole),
- the antidepressants nefazodone and fluoxetine
- quinupristin/dalfopristin,
- cimetidine,
- valproic acid.

Upon co-administration with these drugs, the blood pressure should be monitored and, if necessary, a reduction of the nimodipine dose should be considered.

Nimotop 30 mg / 0.75 ml oral drops, solution contains 48.06 vol% ethanol (alcohol), i.e. up to 4,3 g per daily dose (9 ml). This may be harmful for those suffering from alcoholism or impaired alcohol metabolism and should be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy. The amount of alcohol in this medicinal product may alter the effects of other medicines (see paragraph 4.5, “Interactions with other medicinal products and other forms of interaction”). The amount of alcohol in this medicinal product may impair your ability to drive or to use machines (see paragraph 4.7, “Effects on ability to drive and use machines”).
This medicinal product contains polyoxyl 40 hydrogenated castor oil. This may cause stomach upset and diarrhoea.

The effervescent granules contain saccharose, and thus are not suitable for subjects with hereditary intolerance of fructose, glucose/galactose malabsorption syndrome or saccharose-isomaltase deficit; this medicinal product also contains sodium: it may not be suitable for subjects who must follow a low sodium diet.

4.5. Interactions with other medicinal products and other forms of interaction

Effects of other drugs on nimodipine

Nimodipine is metabolized via the cytochrome P450 3A4 system, located both in the intestinal mucosa and in the liver. Drugs that are known to either inhibit or to induce this enzyme system may therefore alter the first pass or the clearance of nimodipine. The extent as well the duration of interactions should be taken into account when administering nimodipine together with the following drugs:

Rifampicin
From the experience with other calcium antagonists it has to be expected that rifampicin accelerates the metabolism of nimodipine due to enzyme induction. Thus, efficacy of nimodipine could be significantly reduced when concomitantly administered with rifampicin. The use of nimodipine in combination with rifampicin is therefore contraindicated (see paragraph 4.3, “Contraindications”).

Antiepileptic cytochrome P450 3A4 system inducers, such as phenobarbital, phenytoin or carbamazepine.
Previous chronic administration of the antiepileptic drugs phenobarbital, phenytoin or carbamazepine markedly reduces the bioavailability of orally administered nimodipine.

Therefore, the concomitant use of oral nimodipine and these antiepileptic drugs is contraindicated (see paragraph 4.3, “Contraindications).

Cytochrome P450 3A4 system inhibitors
Upon co-administration with the following inhibitors of the cytochrome P450 3A4 system the blood pressure should be monitored and, if necessary, an adaptation in the nimodipine dose should be considered (see paragraph 4.2, “Posology and method of administration”).

Macrolide antibiotics (e.g. erythromycin)
No interaction studies have been carried out between nimodipine and macrolide antibiotics. Certain macrolide antibiotics are known to inhibit the cytochrome P450 3A4 system and the potential for drug interaction cannot be ruled out at this stage. Therefore, macrolide antibiotics should not be used in combination with nimodipine (see “Special warnings”).
Azithromycin, although structurally related to the class of macrolide antibiotic is void of CYP3A4 inhibition.

Anti-HIV protease inhibitors (e.g. ritonavir)
No formal studies have been performed to investigate the potential interaction between nimodipine and anti-HIV protease inhibitors. Drugs of this class have been reported to be potent inhibitors of the cytochrome P450 3A4 system. Therefore, the potential for a marked and clinically relevant increase in nimodipine plasma concentrations upon co-administration with these protease inhibitors cannot be excluded (see paragraph 4.4, “Special warnings”).

Azole anti-mycotics (e.g., ketoconazole)
A formal interaction study investigating the potential of drug interaction between nimodipine and ketoconazole has not been performed. Azole anti-mycotics are known to inhibit the cytochrome P450 3A4 system, and various interactions have been reported for other dihydropyridine calcium antagonists. Therefore, when administered together with oral nimodipine, a substantial increase in systemic bioavailability of nimodipine due to a decreased first-pass metabolism cannot be excluded (see “Special warnings”).

Nefazodone
No formal studies have been performed to investigate the potential interaction between nimodipine and nefazodone. This antidepressant drug has been reported to be a potent inhibitor of the cytochrome P450 3A4. Therefore, the potential for an increase in nimodipine plasma concentrations upon co-administration with nefazodone cannot be excluded (see paragraph 4.4, “Special warnings and precautions for use”).

Fluoxetine
The steady-state concomitant administration of nimodipine with the antidepressant fluoxetine led to about 50% higher nimodipine plasma concentrations. Fluoxetine exposure was markedly decreased, while its active metabolite norfluoxetine was not affected.

Quinupristin/dalfopristin
Based on experience with the calcium-antagonist nifedipine, co-administration of quinupristin/dalfopristin may lead to increased plasma concentrations of nimodipine (see paragraph 4.4, “Special warnings and precautions for use”).

Cimetidine
The simultaneous administration of the H2-antagonist cimetidine can lead to an increase in the plasma nimodipine concentration (see paragraph 4.4, “Special warnings and precautions for use”).

Valproic acid
The simultaneous administration of the anticonvulsant valproic acid can lead to an increase in the plasma nimodipine concentration (see paragraph 4.4, “Special warnings and precautions for use”).

Further interactions
The steady-state concomitant administration of nimodipine and nortryptyline led to a slight decrease in nimodipine exposure with unaffected nortryptyline plasma concentrations.

Effects of nimodipine on other drugs

Antihypertensive drugs
Nimodipine may increase the antihypertensive effect of drugs of this class administered at the same time, including:
- diuretics
- β-blockers
- ACE-inhibitors
- A1 antagonists
- other calcium antagonists
- α-blockers
- PDE5 inhibitors
- α-methyldopa

However, if a combination of this type proves unavoidable particularly careful monitoring of the patient is necessary.

Zidovudine
In a monkey study simultaneous administration of anti-HIV drug zidovudine i.v. and nimodipine bolus i.v. resulted for zidovudine in significantly higher AUC, whereas the distribution volume and clearance were significantly reduced.

Drug-food interactions:

Grapefruit juice:
Grapefruit juice inhibits the oxidative metabolism of dihydropyridine.
The contemporaneous intake of grapefruit juice and nimodipine increases the plasma concentration and duration of action of the latter, due to a decreased first pass metabolism or reduced clearance.
As a consequence, the blood pressure lowering effect may be increased. After intake of grapefruit juice this effect may last for at least 4 days after the last ingestion of grapefruit juice.
Ingestion of grapefruit / grapefruit juice is therefore to be avoided while taking nimodipine

Interactions shown not to exist:

Haloperidol
The concurrent steady-state administration of nimodipine in patients on individual long-term haloperidol treatment did not indicate any potential for mutual interaction.

Concomitant administration of oral nimodipine and diazepam, digoxin, glibenclamide, indomethacin, ranitidine, and warfarin did not reveal any potential for mutual interaction.

4.6. Pregnancy and lactation

Nimotop must not be administered in pregnancy or during breastfeeding (see paragraph 4.3, "Contraindications").

In-vitro fertilisation
In single cases of in-vitro fertilization calcium antagonists have been associated with reversible biochemical changes in the spermatozoa`s head section that may result in impaired sperm function.

4.7. Effects on ability to drive and use machines
In principle the ability to drive and use machines can be impaired in connection with the possible occurrence of dizziness.

4.8. Undesirable effects

Adverse drug reactions (ADRs) based on clinical trials with nimodipine in the indication "Prevention and treatment of ischaemic neurological deficit correlated with cerebral vasospasm" sorted by CIOMS III categories of frequency (placebo-controlled studies: nimodipine N = 703; placebo N = 692; uncontrolled studies: nimodipine N = 2496; status: 31 Aug 2005) are listed below:

Table 1: all adverse reactions to the drug reported by patients in several clinical studies with the indication "Prevention and treatment of ischaemic neurological deficit correlated with cerebral vasospasm".

Clinical description	Common ≥1% to <10%	Not common f≥0.1% to <1%	Rare ≥0.01% to <0.1%.	Very rare <0.01%
Blood and lymphatic system disorders				
Changes in blood cell count		Thrombocytopenia		
Immune system disorders				
Acute hypersensitivity reactions		Allergic reaction Rash		
Nervous system disorders				
Unspecific cerebrovascular symptoms		Headache		
Cardiac disorders				
Unspecific arrhythmias		Tachycardia	Bradycardia	
Vascular disorders				
Unspecific cardiovascular symptoms		Hypotension Vasodilation		
Gastrointestinal disorders				
Gastrointestinal symptoms		Nausea	Ileum	
Hepatobiliary disorders				
Mild to moderate hepatic reactions			Transitory increase in hepatic enzymes	

The adverse reactions correlated with the drug reported in clinical studies with nimodipine with the indication "Prevention and treatment of ischaemic neurological deficit" are shown in table 2, ordered according to the CIOMS III frequency categories (in studies against placebo, 1,594 patients were treated with nimodipine and 1,558 with placebo, and 8,049 patients were

treated with nimodipine in open studies; status at 20 October 2005) and post-marketing data (status: October 2005).
The adverse reactions reported as “common” were observed with a frequency of less than 2%.

Table 2: all adverse reactions to the drug reported by patients in several clinical studies with the indication “Prevention and treatment of ischaemic neurological deficit.

Clinical description	Common ≥1% to <10%	Not common f≥0.1% to <1%	Rare ≥0.01% to <0.1%.	Very rare <0.01%
Immune system disorders				
Acute hypersensitivity reactions		Allergic reaction Rash		
Nervous system disorders				
Unspecific cerebrovascular symptoms		Headache Vertigo		
Unspecific cardiovascular symptoms		Dizziness Hyperkinesia Tremor		
Cardiac disorders				
Unspecific arrhythmias		Palpitations Tachycardia		
Vascular disorders				
Unspecific cardiovascular symptoms	Hypotension Vasodilation	Syncope Oedema		
Gastrointestinal disorders				
Gastrointestinal symptoms		Constipation Diarrhoea Flatulence		

4.9. Overdose

Symptoms of acute overdosage to be anticipated are marked lowering of the blood pressure, tachycardia or bradycardia, and gastrointestinal complaints and nausea.
Treatment: suspend administration of the drug immediately.
Gastric lavage with addition of charcoal should be considered as an emergency therapeutic measure. If there is a marked fall in blood pressure, dopamine or noradrenaline can be administered intravenously. Since no specific antidote is known, subsequent treatment for other side effects should be governed by the most prominent symptoms.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic category: Selective calcium agonist, dihydropyridine derivative
ATC Code: C08CA06
Nimodipine is a calcium antagonist that belongs to the class of 1,4-dihydropyridines, which differs from the other calcium antagonists for its marked selectivity of action in the cerebral district.
With its high lipophilia, nimodipine easily passes the encephalic barrier. In animal studies, nimodipine binds with high affinity and selectivity to the type L Ca^{++} channels, thus blocking intracellular calcium flow across the membrane.

Nimodipine protects the neurons and stabilises their function, promotes cerebral blood flow, and increases tolerance of ischaemia by interactions with the neurone and cerebrovascular receptors linked to the calcium channel.
In pathologies associated with an increase in the intracytoplasmatic calcium flow into the nerve cells, such as during cerebral ischaemia, nimodipine is thought to improve the stability and functional capacity of these cell elements.
The selective blocking of the calcium channels in several brain areas, such as in the hippocampus and the cortex, may explain the positive effect of nimodipine on learning and on the mnemonic deficits observed in several animal models.
The same molecular mechanism probably underlies the cerebral vasodilatory and blood flow promoting effect of nimodipine that has been observed in animals and in man.
Its therapeutic properties are linked to its capacity to inhibit the smooth muscle cell contraction induced by calcium ions.
The use of nimodipine can prevent or eliminate vasoconstrictions induced in-vitro by various vasoactive substances (e.g. serotonin, prostaglandins, and histamine) or by blood and blood degradation products. Nimodipine also has neuropharmacological and psychopharmacological properties. Investigations in patients with acute cerebral blood flow disturbances have shown that nimodipine dilates the cerebral blood vessels and promotes cerebral blood flow. The increase in perfusion is as a rule greater in previously damaged or underperfused brain regions than in healthy regions. Other studies have shown that this does not lead to steal phenomena. The use of nimodipine can achieve a significant reduction in ischaemic neurological deficit and mortality after vasospasm due to subarachnoid haemorrhage of aneurismal origin.
The improvement is significant only in patients with cerebral vasospasm of subarachnoid haemorrhagic origin. Concentrations of nimodipine of up to 12.5 ng/ml have been found in the cerebrospinal fluid of patients treated for subarachnoid haemorrhage.
It has been demonstrated clinically that nimodipine improves memory disorders and concentration in patients with compromised cerebral function.
Other typical symptoms are also favourably influenced, as has been shown by overall clinical impression assessment, individual disorder assessment, observation of behaviour and psychometric testing.

5.2. Pharmacokinetic properties

Absorption

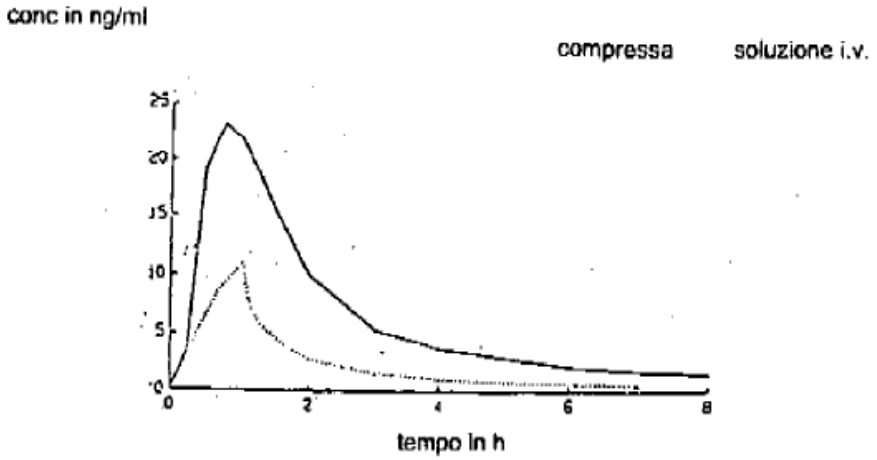
The active substance nimodipine, administered orally, is practically completely absorbed.
The unchanged active substance and its early "first pass" metabolites are detected in plasma as little as 10 -15 min after ingestion of the tablet.
After oral administration of multiple doses (3 x 30 mg/day), plasma concentration peaks (C_{max}) of 7.3-43.2 ng/ml are achieved in elderly subjects, equivalent to 7.3-43.2 ng/ml, and are reached after 0.6-1.6 h (t_{max}).
Single doses of 30 mg and 60 mg in young subjects result in mean peak plasma concentrations of 16 ± 8 ng/ml and 31 ± 12 ng/ml respectively.
The peak plasma concentration and the area under the concentration/time curve increase proportionally to the dose up to the highest dose under test (90mg).
Mean plasma concentrations of 17.6 – 26.6 ng/ml are reached at steady state after continuous i.v. infusion of 0.03 ng/kg/h. After i.v. bolus, the nimodipine plasma concentrations decline in a biphasic way, with half-life at 5-10 minutes and at around 60 minutes. The distribution volume (Vss in the two compartment model) for i.v. administration is calculated to be 0.9 - 1.6 l/kg body weight. The total systemic clearance is 0.6 - 1.9 l/h/kg.

Protein binding and distribution

97-99% of the nimodipine binds to the plasma proteins.
In experimental animals treated with ^{14}C labelled nimodipine, the radioactivity passed the placental barrier.

A similar distribution is likely in women, although there is no experimental evidence to this effect.
In the rat, nimodipine and/or its metabolites appear in milk at a far higher concentration than in the plasma of the mother. In women, unchanged drug appears in breast milk at concentrations of the same order of magnitude as in the mother's plasma.
After oral and intravenous administration, nimodipine can be dosed in the cerebrospinal fluid at concentrations equivalent to about 0.5% of those found in the plasma.
These roughly correspond to the concentrations of free active substance in the plasma.

Metabolism, elimination and excretion
Nimodipine is metabolised through the cytochrome P450 3A4 system, mainly by the dehydrogenation of the dihydropyridine ring and oxidative breakdown of the ester, which, with hydroxylation of the 2 and 6 ethyl groups, and the glucuronidation, represent the subsequent important metabolic stages.
The three main metabolites in the plasma possess insignificant or no residual therapeutic activity.
The effects of induction and inhibition on the hepatic enzymes are unknown. In man, the metabolites are excreted about 50% through the renal emunctory and 30% in the bile.
The elimination kinetics are linear. The half-life for nimodipine is between 1.1 and 1.7 hours.
The terminal half-life of 5 - 10 hours is not relevant for the purpose of establishing the dosage interval.



The mean plasma concentration curve for nimodipine after administration of 30 mg in tablet formulation, and after i.v. infusion of 0.015 mg/kg/hour (n=24 elderly volunteers).

Bioavailability
Because of the considerable first-pass metabolism (about 85 - 95%) the absolute bioavailability is 5 - 15%.

5.3. Preclinical safety data
Preclinical data based on conventional studies with single and repeated doses do not reveal any particular risks for human beings in terms of toxicity, genotoxicity, carcinogenesis or fertility, whether male or female. In pregnant rats, doses of 30 mg/kg/day or more inhibited foetal growth, causing a decrease in the weight of the foetus. A dose of 100 mg/kg/day was lethal for the foetus. There was no evidence of teratogenicity. In rabbits, no embryotoxicity or teratogenicity was observed with doses up to 10 mg/kg/day. In a peri-postnatal study in rats,

mortality and delayed physical development were observed at doses of 10 g/kg/day or more. These results were not confirmed in subsequent studies.

Acute toxicity

Animal species	sex	Administration route	LD_{50} (mg/kg)	Confidence interval for $p \leq 0.05$
Mouse	M	oral	3562	(2746-4417)
Mouse	M	i.v.	33	(28-38)
Rat	M	oral	6599	(5118-10003)
Rat	M	i.v.	16	(14-18)
Rabbit	F	oral	about 5000	
Rabbit	F	i.v.	about 2.5	
Dog	M - F	oral	between 1000 and 2000	
Dog	M - F	i.v.	about 4.5	

The difference in the LD_{50} values after oral and intravenous administration indicates that absorption of the active substance is incomplete or delayed after oral administration of high doses in the oral suspension formulation.
The symptoms of poisoning after oral administration were only observed in the mouse and the rat, and consisted of mild cyanosis, severe reduction in motility, and dyspnoea.
After i.v. administration these signs of poisoning, associated with tonic-clonic seizures, were observed in all the species studied.

Subchronic toxicity:
Studies performed in the dog at a dose of 10 mg/kg per os induced a fall in body weight, decreased haemotocrit, haemoglobin and erythrocytes, increased heart rate and alterations in blood pressure.

Chronic tolerability studies
Oral dosages of up to 90 mg/kg/day for two years were well tolerated in the mouse.
In a one-year study on dogs the systemic tolerability of doses of up to 6.25 mg nimodipine/kg/day was investigated. Doses up to 2.5 mg/kg proved harmless, while 6.25 mg/kg gave rise to electrocardiographic changes due to disturbances in myocardial blood flow. However, no histopathological alterations in the heart were found at this dose.

Studies on reproduction toxicity

Fertility studies in rats

Doses of up to 30 mg/kg/day did not affect the fertility of male and female rats, or that of subsequent generations.

Embryotoxicity studies
Administration of 10 mg/kg/day to pregnant rats appeared to have no dangerous effects, while doses of 30 mg/kg/day and more inhibited growth, resulting in reduced foetal weight and, at 100 mg/kg/day, an increase in intrauterine embryonic deaths.
Embryotoxicity studies in the rabbit with oral doses of up to 10 mg/kg/day appeared to have no teratogenic or embryotoxic effects.

Perinatal and postnatal development in rats
To evaluate perinatal and postnatal development, studies were performed on rats with doses of up to 30 mg/kg/day.
In a study with 10 mg/kg/day and more, an increase in both perinatal and postnatal mortality, and delayed physical development were observed. These results were not confirmed in subsequent studies.

Specific tolerability studies

Cancerogenesis
In a lifetime study of rats treated for 2 years with dosages of up to 1800 parts per million (about 90 mg/kg/day) in feed, no oncogenic potential was observed.
Similar results were obtained in mice treated for 21 months in a long-term study with 500 mg/kg/day per os.

Mutagenesis
Nimodipine has been tested in many mutagenesis studies, which detected no gene or chromosome mutation effects of note.

6. Pharmaceutical information

6.1. List of excipients:
coated tablets
microgranular cellulose, povidone, crospovidone, magnesium stearate, corn starch, hypromellose, macrogol 4000, titanium dioxide (E171), yellow iron oxide (E172).

oral drops, solution.
Polyoxyl 40 hydrogenated castor oil, ethyl alcohol

effervescent granules:
povidone, citric acid, sodium (mono) citrate, sodium bicarbonate, sodium carbonate, orange flavouring, saccharose, sodium saccharin, dried orange juice, E 110 subset yellow, sodium docusate.

6.2. Incompatibilities

None known.

6.3. Shelf life
coated tablets: 5 years
oral drops, solution: 5 years
effervescent granules: 2 years

6.4. Special precautions for storage

coated tablets: none
oral drops, solution: protect from light / do not store in a refrigerator
effervescent granules: none

6.5. Nature and content of container

tablets 36 tablets
PVC/aluminium of PVC-PVDC/aluminium or PP blister.

oral drops, solution: 25 ml bottle
brown glass bottle with screw cap and glass dropper.

effervescent granules: 36 sachets
box in printed cardboard containing 36 paper/polythene/aluminium polythene sachets in pairs.

6.6 Instructions for use and handling
No specific instructions

7. Marketing authorisation holder
Bayer S.p.A. Viale Certosa 130 – Milan, Italy

8. Number of marketing authorisation

NIMOTOP 30 mg coated tablets	MA 026403016
NIMOTOP 30 effervescent granules	MA 026403067
NIMOTOP 30 mg/0.75 ml oral drops, solution	MA 026403055

:

9. Date of first authorisation/renewal of authorisation
Tablets, oral drops, solution
First authorisation: 27 July 1987 (on sale since October 1987)
Renewal of authorisation: June 2005

Effervescent granules:
First authorisation: 31 October 1994 (on sale since 1 April 1996)
Renewal of authorisation: June 2005

10. Date of revision of text:
February 2007.