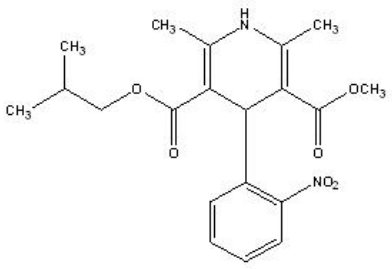
NISOLDIPINE - nisoldipine tablet, film coated, extended release
Physicians Total Care, Inc.

DESCRIPTION

Nisoldipine is an extended-release tablet dosage form of the dihydropyridine calcium channel blocker nisoldipine. Nisoldipine is (±)-Isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(*o*-nitrophenyl)-3,5-pyridinedicarboxylate, $C_{20}H_{24}N_2O_6$, and has the structural formula:



Nisoldipine is a yellow crystalline powder, practically insoluble in water but soluble in acetone, ethanol and methanol. It has a molecular weight of 388.4. Nisoldipine extended-release tablets contain 20 mg, 30 mg or 40 mg of nisoldipine for once-a-day oral administration.

Inactive ingredients include: colloidal silicon dioxide, hydroxypropyl cellulose, hypromellose, lactose monohydrate and magnesium stearate. In addition, the following product specific coloring agents are employed:

20 mg—	FD&C Blue No. 2 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, hypromellose, polydextrose, polyethylene glycol, titanium dioxide and triacetin.
30 mg—	polydextrose, polyethylene glycol, red iron oxide, titanium dioxide, triacetin and yellow iron oxide.
40 mg—	D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, hypromellose, polydextrose, polyethylene glycol and titanium dioxide.

CLINICAL PHARMACOLOGY

Mechanism of Action

Nisoldipine is a member of the dihydropyridine class of calcium channel antagonists (calcium ion antagonists or slow channel blockers) that inhibit the transmembrane influx of calcium into vascular smooth muscle and cardiac muscle. It reversibly competes with other dihydropyridines for binding to the calcium channel. Because the contractile process of vascular smooth muscle is dependent upon the movement of extracellular calcium into the muscle through specific ion channels, inhibition of the calcium channel results in dilation of the arterioles. *In vitro* studies show that the effects of nisoldipine on contractile processes are selective, with greater potency on vascular smooth muscle than on cardiac muscle. Although, like other dihydropyridine calcium channel blockers, nisoldipine has negative inotropic effects, *in vitro*, studies conducted in intact anesthetized animals have shown that the vasodilating effect occurs at doses lower than those that affect cardiac contractility.

The effect of nisoldipine on blood pressure is principally a consequence of a dose-related decrease of peripheral vascular resistance. While nisoldipine, like other dihydropyridines, exhibits a mild diuretic effect, most of the antihypertensive activity is attributed to its effect on peripheral vascular resistance.

Pharmacokinetics and Metabolism

Nisoldipine pharmacokinetics are independent of the dose in the range of 20 to 60 mg, with plasma concentrations proportional to dose. Nisoldipine accumulation, during multiple dosing, is predictable from a single dose.

Nisoldipine is relatively well absorbed into the systemic circulation with 87% of the radiolabeled drug recovered in urine and feces. The absolute bioavailability of nisoldipine is about 5%. Nisoldipine's low bioavailability is due, in part, to pre-systemic metabolism in the gut wall, and this metabolism decreases from the proximal to the distal parts of the intestine. Food with a high fat content has a pronounced effect on the release of nisoldipine from the coat-core formulation and results in a significant increase in peak concentration (C_{max}) by up to 300%. Total exposure, however, is decreased about 25%, presumably because more of the drug is released proximally. This effect appears to be specific for nisoldipine in the controlled release formulation, as a less pronounced food effect was seen with the immediate release tablet. Concomitant intake of a high fat meal with nisoldipine extended-release should be avoided.

Maximal plasma concentrations of nisoldipine are reached 6 to 12 hours after dosing. The terminal elimination half-life (reflecting post absorption clearance of nisoldipine) ranges from 7 to 12 hours. C_{max} and AUC increase by factors of approximately 1.3 and 1.5, respectively, from first dose to steady-

state. After oral administration, the concentration of (+) nisoldipine, the active enantiomer, is about 6 times higher than the (-) inactive enantiomer. The plasma protein binding of nisoldipine is very high, with less than 1% unbound over the plasma concentration range of 100 ng/mL to 10 mcg/mL.

Nisoldipine is highly metabolized; 5 major urinary metabolites have been identified. Although 60 to 80% of an oral dose undergoes urinary excretion, only traces of unchanged nisoldipine are found in urine. The major biotransformation pathway appears to be the hydroxylation of the isobutyl ester. A hydroxylated derivative of the side chain, present in plasma at concentrations approximately equal to the parent compound, appears to be the only active metabolite, and has about 10% of the activity of the parent compound. Cytochrome P_{450} enzymes are believed to play a major role in the metabolism of nisoldipine. The particular isoenzyme system responsible for its metabolism has not been identified, but other dihydropyridines are metabolized by cytochrome P_{450} IIIA4. Nisoldipine should not be administered with grapefruit juice as this has been shown, in a study of 12 subjects, to interfere with nisoldipine metabolism, resulting in a mean increase in C_{max} of about 3-fold (ranging up to about 7-fold) and AUC of almost 2-fold (ranging up to about 5-fold). A similar phenomenon has been seen with several other dihydropyridine calcium channel blockers.

Special Populations

Renal Dysfunction

Because renal elimination is not an important pathway, bioavailability and pharmacokinetics of nisoldipine extended-release were not significantly different in patients with various degrees of renal impairment. Dosing adjustments in patients with mild to moderate renal impairment are not necessary.

Geriatric

Elderly patients have been found to have 2 to 3 fold higher plasma concentrations (C_{max} and AUC) than young subjects. This should be reflected in more cautious dosing (see DOSAGE AND ADMINISTRATION).

Hepatic Insufficiency

In patients with liver cirrhosis given 10 mg nisoldipine extended-release, plasma concentrations of the parent compound were 4 to 5 times higher than those in healthy young subjects. Lower starting and maintenance doses should be used in cirrhotic patients (see DOSAGE AND ADMINISTRATION).

Gender and Race

The effect of gender or race on the pharmacokinetics of nisoldipine has not been investigated.

Disease States

Hypertension does not significantly alter the pharmacokinetics of nisoldipine.

Pharmacodynamics

Hemodynamic Effects

Administration of a single dose of nisoldipine leads to decreased systemic vascular resistance and blood pressure with a transient increase in heart rate. The change in heart rate is greater with immediate release nisoldipine preparations. The effect on blood pressure is directly related to the initial degree of elevation above normal. Chronic administration of nisoldipine results in a sustained decrease in vascular resistance and small increases in stroke index and left ventricular ejection fraction. A study of the immediate release formulation showed no effect of nisoldipine on the renin-angiotensin-aldosterone system or on plasma norepinephrine concentration in normals. Changes in blood pressure in hypertensive patients given nisoldipine extended-release were dose related over the range of 10 to 60 mg/day.

Nisoldipine does not appear to have significant negative inotropic activity in intact animals or humans, and did not lead to worsening of clinical heart failure in three small studies of patients with asymptomatic and symptomatic left ventricular dysfunction. There is little information, however, in patients with severe congestive heart failure, and all calcium channel blockers should be used with caution in any patient with heart failure.

Electrophysiologic Effects

Nisoldipine has no clinically important chronotropic effects. Except for mild shortening of sinus cycle, SA conduction time and AH intervals, single oral doses up to 20 mg of immediate release nisoldipine did not significantly change other conduction parameters. Similar electrophysiologic effects were seen with single iv doses, which could be blunted in patients pre-treated with beta-blockers. Dose and plasma level related flattening or inversion of T-waves have been observed in a few small studies. Such reports were concentrated in patients receiving rapidly increased high doses in one study; the phenomenon has not been a cause of safety concern in large clinical trials.

Clinical Studies in Hypertension

The antihypertensive efficacy of nisoldipine extended-release was studied in five double-blind, placebo-controlled, randomized studies, in which over 600 patients were treated with nisoldipine extended-release as monotherapy and about 300 with placebo; 4 of the 5 studies compared 2 or 3 fixed doses while the fifth allowed titration from 10 to 40 mg. Once daily administration of nisoldipine extended-release produced sustained reductions in systolic and diastolic blood pressures over the 24 hour dosing interval in both supine and standing positions. The mean placebo-subtracted reductions in

supine systolic and diastolic blood pressure at trough, 24 hours post-dose, in these studies, are shown below. Changes in standing blood pressure were similar:

MEAN SUPINE THROUGH SYSTOLIC AND DIASTOLIC BLOOD PRESSURE CHANGES (mm Hg)

Nisoldipine Extended-release Dose (mg/day)	10 mg	20 mg	30 mg	40 mg	60 mg	10 to 40 mg titrated
Systolic	8	11	11	14	15	15
Diastolic	3	5	7	7	10	8

In patients receiving atenolol, supine blood pressure reductions with nisoldipine extended-release at 20, 40 and 60 mg once daily were 12/6, 19/8 and 22/10 mm Hg, respectively. The sustained antihypertensive effect of nisoldipine extended-release was demonstrated by 24 hour blood pressure monitoring and examination of peak and trough effects. The trough/peak ratios ranged from 70 to 100% for diastolic and systolic blood pressure. The mean change in heart rate in these studies was less than one beat per minute. In 4 of the 5 studies, patients received initial doses of 20 mg to 30 mg nisoldipine extended-release without incident (excessive effects on blood pressure or heart rate). The fifth study started patients on lower doses of nisoldipine extended-release.

Patient race and gender did not influence the blood pressure lowering effect of nisoldipine extended-release. Despite the higher plasma concentration of nisoldipine in the elderly, there was no consistent difference in their blood pressure response except that the 10 mg dose was somewhat more effective than in non-elderly patients. No postural effect on blood pressure was apparent and there was no evidence of tolerance to the antihypertensive effect of nisoldipine extended-release in patients treated for up to one year.

INDICATIONS AND USAGE

Nisoldipine extended-release tablets are indicated for the treatment of hypertension. They may be used alone or in combination with other antihypertensive agents.

CONTRAINDICATIONS

Nisoldipine extended-release tablets are contraindicated in patients with known hypersensitivity to dihydropyridine calcium channel blockers.

WARNINGS

Increased Angina and/or Myocardial Infarction In Patients With Coronary Artery Disease

Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed increased frequency, duration and/or severity of angina, or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been established. In controlled studies of nisoldipine extended-release in patients with angina this was seen about 1.5% of the time in patients given nisoldipine, compared with 0.9% in patients given placebo.

PRECAUTIONS

General

Hypotension

Because nisoldipine, like other vasodilators, decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of nisoldipine extended-release is recommended. Close observation is especially important for patients already taking medications that are known to lower blood pressure. Although in most patients the hypotensive effect of nisoldipine extended-release is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment.

Congestive Heart Failure

Although acute hemodynamic studies of nisoldipine in patients with NYHA Class II to IV heart failure have not demonstrated negative inotropic effects, safety of nisoldipine extended-release in patients with heart failure has not been established. Caution therefore should be exercised when using nisoldipine extended-release in patients with heart failure or compromised ventricular function, particularly in combination with a beta-blocker.

Patients with Hepatic Impairment

Because nisoldipine is extensively metabolized by the liver and, in patients with cirrhosis, it reaches blood concentrations about 5 times those in normals, nisoldipine extended-release should be administered cautiously in patients with severe hepatic dysfunction (see DOSAGE AND ADMINISTRATION).

Information for Patients

Nisoldipine is an extended release tablet and should be swallowed whole. Tablets should not be

chewed, divided or crushed. Nisoldipine extended-release tablets should not be administered with a high fat meal. Grapefruit juice, which has been shown to increase significantly the bioavailability of nisoldipine and other dihydropyridine type calcium channel blockers, should not be taken with nisoldipine extended-release.

Laboratory Tests

Nisoldipine extended-release is not known to interfere with the interpretation of laboratory tests.

Drug Interactions

A 30 to 45% increase in AUC and C_{max} of nisoldipine was observed with concomitant administration of cimetidine 400 mg twice daily. Ranitidine 150 mg twice daily did not interact significantly with nisoldipine (AUC was decreased by 15 to 20 %). No pharmacodynamic effects of either histamine H_2 receptor antagonist were observed.

Coadministration of phenytoin with 40 mg nisoldipine extended-release tablets in epileptic patients lowered the nisoldipine plasma concentrations to undetectable levels. Coadministration of nisoldipine extended-release with phenytoin or any known CYP3A4 inducer should be avoided and alternative antihypertensive therapy should be considered. Pharmacokinetic interactions between nisoldipine and beta-blockers (atenolol, propranolol) were variable and not significant. Propranolol attenuated the heart rate increase following administration of immediate release nisoldipine. The blood pressure effect of nisoldipine extended-release tended to be greater in patients on atenolol than in patients on no other antihypertensive therapy. Quinidine at 648 mg bid decreased the bioavailability (AUC) of nisoldipine by 26%, but not the peak concentration. The immediate release, but not the coat-core formulation of nisoldipine increased plasma quinidine concentrations by about 20%. This interaction was not accompanied by ECG changes and its clinical significance is not known. No significant interactions were found between nisoldipine and warfarin or digoxin.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Dietary administration of nisoldipine to male and female rats for up to 24 months (mean doses up to 82 and 111 mg/kg/day, 16 and 19 times the maximum recommended human dose {MRHD} on a mg/m^2 basis, respectively) and female mice for up to 21 months (mean doses of up to 217 mg/kg/day, 20 times the MRHD on a mg/m^2 basis) revealed no evidence of tumorigenic effect of nisoldipine. In male mice receiving a mean dose of 163 mg nisoldipine/kg/day (16 times the MRHD of 60 mg/day on a mg/m^2 basis), an increased frequency of stomach papilloma, but still within the historical range, was observed. No evidence of stomach neoplasia was observed at lower doses (up to 58 mg/kg/day). Nisoldipine was negative when tested in a battery of genotoxicity assays including the Ames test and the CHO/HGRPT assay for mutagenicity and the *in vivo* mouse micronucleus test and *in vitro* CHO cell test for clastogenicity.

When administered to male and female rats at doses of up to 30 mg/kg/day (about 5 times the MRHD on a mg/m^2 basis) nisoldipine had no effect on fertility.

Pregnancy

Category C

Nisoldipine was neither teratogenic nor fetotoxic at doses that were not maternally toxic. Nisoldipine was fetotoxic but not teratogenic in rats and rabbits at doses resulting in maternal toxicity (reduced maternal body weight gain). In pregnant rats, increased fetal resorption (postimplantation loss) was observed at 100 mg/kg/day and decreased fetal weight was observed at both 30 and 100 mg/kg/day. These doses are, respectively, about 5 and 16 times the MRHD when compared on a mg/m^2 basis. In pregnant rabbits, decreased fetal and placental weights were observed at a dose of 30 mg/kg/day, about 10 times the MRHD when compared on a mg/m^2 basis. In a study in which pregnant monkeys (both treated and control) had high rates of abortion and mortality, the only surviving fetus from a group exposed to a maternal dose of 100 mg nisoldipine/kg/day (about 30 times the MRHD when compared on a mg/m^2 basis) presented with forelimb and vertebral abnormalities not previously seen in control monkeys of the same strain. There are no adequate and well controlled studies in pregnant women. Nisoldipine extended-release should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether nisoldipine is excreted in human milk. Because many drugs are excreted in human milk, a decision should be made to discontinue nursing, or to discontinue nisoldipine extended-release, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Clinical studies of nisoldipine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Patients over 65 are expected to develop higher plasma concentrations of nisoldipine. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

More than 6,000 patients world-wide have received nisoldipine in clinical trials for the treatment of hypertension, either as the immediate release or the nisoldipine extended-release formulation. Of about 1,500 patients who received nisoldipine extended-release in hypertension studies, about 55% were exposed for at least 2 months and about one third were exposed for over 6 months, the great majority at doses of 20 to 60 mg daily.

Nisoldipine extended-release is generally well-tolerated. In the U.S. clinical trials of nisoldipine extended-release in hypertension, 10.9% of the 921 nisoldipine extended-release patients discontinued treatment due to adverse events compared with 2.9% of 280 placebo patients. The frequency of discontinuations due to adverse experiences was related to dose, with a 5.4% discontinuation rate at 10 mg daily and a 10.9% discontinuation rate at 60 mg daily.

The most frequently occurring adverse experiences with nisoldipine extended-release are those related to its vasodilator properties; these are generally mild and only occasionally lead to patient withdrawal from treatment. The table below, from U.S. placebo-controlled parallel dose response trials of nisoldipine extended-release using doses from 10 to 60 mg once daily in patients with hypertension, lists all of the adverse events, regardless of the causal relationship to nisoldipine extended release, for which the overall incidence on nisoldipine extended-release was both >1% and greater with nisoldipine extended-release than with placebo.

Adverse Event	Nisoldipine (%) (n=663)	Placebo (%) (n=280)
Peripheral Edema	22	10
Headache	22	15
Dizziness	5	4
Pharyngitis	5	4
Vasodilation	4	2
Sinusitis	3	2
Palpitation	3	1
Chest Pain	2	1
Nausea	2	1
Rash	2	1

Only peripheral edema and possibly dizziness appear to be dose related.

Adverse Event		Nisoldipine Extended-release				
	Placebo	10 mg	20 mg	30 mg	40 mg	60 mg
(Rates in %)	n=280	n=30	n=170	n=105	n=139	n=137
Peripheral Edema	10	7	15	20	27	29
Dizziness	4	7	3	3	4	10

The common adverse events occurred at about the same rate in men as in women, and at a similar rate in patients over age 65 as in those under that age, except that headache was much less common in older patients. Except for peripheral edema and vasodilation, which were more common in whites, adverse event rates were similar in blacks and whites.

The following adverse events occurred in ≤1% of all patients treated for hypertension in U.S. and foreign clinical trials, or with unspecified incidence in other studies. Although a causal relationship of nisoldipine extended-release to these events cannot be established, they are listed to alert the physician to a possible relationship with nisoldipine extended-release treatment.

Body As A Whole: cellulitis, chills, facial edema, fever, flu syndrome, malaise

Cardiovascular: atrial fibrillation, cerebrovascular accident, congestive heart failure, first degree AV block, hypertension, hypotension, jugular venous distension, migraine, myocardial infarction, postural hypotension, ventricular extrasystoles, supraventricular tachycardia, syncope, systolic ejection murmur, T wave abnormalities on ECG (flattening, inversion, nonspecific changes), venous insufficiency

Digestive: abnormal liver function tests, anorexia, colitis, diarrhea, dry mouth, dyspepsia, dysphagia, flatulence, gastritis, gastrointestinal hemorrhage, gingival hyperplasia, glossitis, hepatomegaly, increased appetite, melena, mouth ulceration

Endocrine: diabetes mellitus, thyroiditis

Hemic and Lymphatic: anemia, ecchymoses, leukopenia, petechiae

Metabolic and Nutritional: gout, hypokalemia, increased serum creatine kinase, increased nonprotein nitrogen, weight gain, weight loss

Musculoskeletal: arthralgia, arthritis, leg cramps, myalgia, myasthenia, myositis, tenosynovitis

Nervous: abnormal dreams, abnormal thinking and confusion, amnesia, anxiety, ataxia, cerebral ischemia, decreased libido, depression, hypesthesia, hypertonia, insomnia, nervousness, paresthesia, somnolence, tremor, vertigo

Respiratory: asthma, dyspnea, end inspiratory wheeze and fine rales, epistaxis, increased cough, laryngitis, pharyngitis, pleural effusion, rhinitis, sinusitis

Skin and Appendages: acne, alopecia, dry skin, exfoliative dermatitis, fungal dermatitis, herpes simplex, herpes zoster, maculopapular rash, pruritus, pustular rash, skin discoloration, skin ulcer, sweating, urticaria

Special Senses: abnormal vision, amblyopia, blepharitis, conjunctivitis, ear pain, glaucoma, itchy eyes, keratoconjunctivitis, otitis media, retinal detachment, tinnitus, watery eyes, taste disturbance, temporary unilateral loss of vision, vitreous floater

Urogenital: dysuria, hematuria, impotence, nocturia, urinary frequency, increased BUN and serum creatinine, vaginal hemorrhage, vaginitis.

The following postmarketing event has been reported very rarely in patients receiving nisoldipine extended-release: systemic hypersensitivity reaction which may include one or more of the following; angioedema, shortness of breath, tachycardia, chest tightness, hypotension, and rash. A definite causal relationship with nisoldipine extended-release has not been established. An unusual event observed with immediate release nisoldipine but not observed with nisoldipine extended-release was one case of photosensitivity. Gynecomastia has been associated with the use of calcium channel blockers.

OVERDOSAGE

There is no experience with nisoldipine overdosage. Generally, overdosage with other dihydropyridines leading to pronounced hypotension calls for active cardiovascular support including monitoring of cardiovascular and respiratory function, elevation of extremities, judicious use of calcium infusion, pressor agents and fluids. Clearance of nisoldipine would be expected to be slowed in patients with impaired liver function. Since nisoldipine is highly protein bound, dialysis is not likely to be of any benefit; however, plasmapheresis may be beneficial.

DOSAGE AND ADMINISTRATION

The dosage of nisoldipine extended-release tablets must be adjusted to each patient's needs. Therapy usually should be initiated with 20 mg orally once daily, then increased by 10 mg per week or longer intervals, to attain adequate control of blood pressure. Usual maintenance dosage is 20 to 40 mg once daily. Blood pressure response increases over the 10 to 60 mg daily dose range but adverse event rates also increase. Doses beyond 60 mg once daily are not recommended. Nisoldipine extended-release tablets have been used safely with diuretics, ACE inhibitors, and beta-blocking agents. Patients over age 65, or patients with impaired liver function are expected to develop higher plasma concentrations of nisoldipine. Their blood pressure should be monitored closely during any dosage adjustment. A starting dose not exceeding 10 mg daily is recommended in these patient groups. Nisoldipine extended-release tablets should be administered orally once daily. Administration with a high fat meal can lead to excessive peak drug concentration and should be avoided. Grapefruit products should be avoided before and after dosing. Nisoldipine is an extended release dosage form and tablets should be swallowed whole, not bitten, divided or crushed.

HOW SUPPLIED

Nisoldipine Extended-release Tablets are available containing 40 mg of nisoldipine.

The 40 mg tablets are yellow, film-coated, round, unscored tablets debossed with **M** on one side of the tablet and **N** over **24** on the other side. They are available as follows:

NDC 54868-5931-0
bottles of 10 tablets

NDC 54868-5931-1
bottles of 30 tablets

Store at 20° to 25°C (68° to 77°F). [See USP for Controlled Room Temperature.]

Protect from light and moisture.

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

Mylan Pharmaceuticals Inc.
Morgantown, WV 26505

REVISED JUNE 2008
NLDP:R2

Relabeling and Repackaging by:
Physicians Total Care, Inc.
Tulsa, Oklahoma 74146

PRINCIPAL DISPLAY PANEL - 40 mg

NISOLDIPINE
EXTENDED-RELEASE
TABLETS
40 mg

(Rx only)

Each film-coated, extended-release tablet contains:
Nisoldipine . . . . . 40 mg

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

Keep container tightly closed.

Keep this and all medication out of the reach of children.

Store at 20° to 25°C (68° to 77°F). [See USP for Controlled Room Temperature.]

Protect from light and moisture.

Usual Dosage: See accompanying prescribing information.

NISOLDIPINE

nisoldipine tablet, film coated, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:54868-5931(NDC:0378-2224)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NISOLDIPINE (UNII: 4I8HAB65SZ) (NISOLDIPINE - UNII:4I8HAB65SZ)	NISOLDIPINE	40 mg

Inactive Ingredients	
Ingredient Name	**Strength**
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
HYDROXYPROPYL CELLULOSE (UNII: RFW2ET671P)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
POLYDEXTROSE (UNII: VH2XOU12IE)	
POLYETHYLENE GLYCOLS (UNII: 3WJQ0SDW1A)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	YELLOW	**Score**	no score
Shape	ROUND	**Size**	10mm
Flavor		**Imprint Code**	M;N;24
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-5931-0	10 in 1 BOTTLE, PLASTIC		
2	NDC:54868-5931-1	30 in 1 BOTTLE, PLASTIC		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA079051	08/29/2008	

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

Name	Address	ID/FEI	Business Operations
Physicians Total Care, Inc.		194123980	relabel, repack

Revised: 5/2012 Physicians Total Care, Inc.