

Package Insert**NIFED SOFT**

NF06P-0

Description

Nifed Soft Capsule : Oblong, orange soft gelatin capsule

Composition

Each soft capsule contains Nifedipine 10 mg

Actions and Pharmacology

Nifedipine is a calcium-ion influx inhibitor (slow-channel blocking agent). It is thought to inhibit calcium ion entry across cell membranes in cardiac and vascular smooth muscle cells and hence reduce intracellular calcium concentration. Nifedipine is a potent peripheral vasodilator. Administration of nifedipine results primarily in vasodilatation, with reduced peripheral resistance, blood pressure, and afterload, increased coronary blood flow, and a reflex increase in heart rate. This in turn results in an increase in myocardial oxygen supply and cardiac output. It has little or no action at the SA or AV nodes, and negative inotropic effect is masked by the reflex increase in heart rate.

Indications

Nifedipine is used in the management of:

- Classic and vasospastic angina pectoris.
- Essential hypertension.

Contraindications

Not recommended for patients with severe hypotension. Risk-benefit should be considered when the following medical problems exist: Severe aortic stenosis, bradycardia or heart failure, cardiogenic shock, hepatic function impairment, mild to moderate hypotension, acute myocardial infarction with pulmonary congestion, renal function impairment and sensitivity to the calcium channel blocker prescribed.

Precautions

- Adequate and well-controlled studies in human have not been done. Animal studies have shown nifedipine to be teratogenic and reduce fertility.
- Nifedipine should not be given to nursing mothers since it has been detected in breast milk.
- Prescribers and pharmacists should be aware that capsule and tablet preparations of nifedipine have different absorption and consequently pharmacological action profile.
- An inappropriate substitution of one preparation for the other could lead to harmful effects or delay in responses.
- Severe hypotension and other side-effects have been reported in patients inadvertently receiving nifedipine capsules instead of tablets.
- Nifedipine may be used in combination with beta-blocking drugs and other antihypertensive agents but the possibility of an additive effect resulting in postural hypotension should be borne in mind. Nifedipine will not prevent possible rebound effects after cessation of other antihypertensive therapy.
- Ischaemic pain has been reported in a small proportion of patients within 30 to 60 minutes of the introduction of nifedipine therapy. Although a 'steal' effect has not been demonstrated, patients experiencing this effect should discontinue nifedipine. The use of nifedipine in diabetic patients may require adjustment of their control.
- The antihypertensive effect of nifedipine may be potentiated by simultaneous administration of cimetidine. When used in combination with nifedipine, serum quinidine levels have been shown to be suppressed regardless of dosage of quinidine.

Warning

Several well documented studies have described profound hypotension, myocardial infarction and death when immediate release nifedipine capsules are used sublingually for acute reduction of blood pressure.

Main Side/Adverse Effects

Peripheral edema, headache, dizziness, flushing, nausea, constipation, unusual tiredness or weakness, arthritis, transient blindness, increase in ischaemic chest pain at the start of treatment, reflex tachycardia, abnormalities in liver function, gingival hyperplasia, bradycardia and hypotension.

Drug Interactions

- Drug interactions may occur when administered concurrently with the following medications: Anaesthetics, hydrocarbon inhalation, NSAIDs, beta-adrenergic blocking agents, quinidine, cimetidine, oestrogen, anticoagulants, lithium, prazosin and sympathomimetics.
- Experience in over 1400 patients, in a non-comparative clinical trial has shown that concomitant administration of nifedipine and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.
- Long-acting nitrates: Nifedipine may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
- Digoxin: Since there have been isolated reports of patients with elevated digoxin levels, and there is a possible interaction between digoxin and nifedipine, it is recommended that digoxin levels be monitored when initiating, adjusting and discontinuing nifedipine to avoid possible over or under digitalization.
- Coumarin anticoagulants: There have been rare reports of increased prothrombin time in patients taking coumarin anticoagulants to whom nifedipine was administered. However, the relationship to nifedipine therapy is uncertain.
- Cimetidine: A study in six healthy volunteers has shown a significant increase peak nifedipine plasma levels (50%) and area-under-the-curve (74%) after a one week course of cimetidine on hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of nifedipine. If nifedipine therapy is initiated in a patient currently receiving cimetidine, cautious titration is advised.
- Quinidine: There have been rare reports of an interaction between quinidine and nifedipine (with a decrease plasma level of quinidine).

Package Insert

Overdosage

Clinical features :

Bradycardia, hypotension, ECG changes, metabolic acidosis, hyperglycaemia and coma.

Treatment for Overdosage :

Treat overdosage by gastric lavage, if appropriate; supportive therapy is recommended.

Administer 10 - 20 ml 10% calcium gluconate and if hypotension does not respond to plasma expanders, give dopamine 5 - 20 µg/kg/min, dobutamine 5 - 40 µg/kg/min or isoprenaline 0.5 - 50 µg/min.

Reports of overdosage are limited and symptoms are not necessarily dose-related. Severe hypotension, bradycardia and unconsciousness have been observed. Gastric lavage and charcoal instillation have been employed. Intravenous calcium gluconate or calcium chloride appear most helpful, with intravenous atropine for bradycardia. Metaraminol has been beneficially combined with calcium salts in the experimental situation.

Dosage and Administration

Adults : Oral, initially 10 mg three times daily, the dosage being increased gradually over a seven to fourteen-day period as needed and tolerated. Maximum 180 mg daily.
For oral administration, the capsules should be taken with a little fluid during or after food. The recommended dose is one 10 mg capsule three times daily with subsequent titration of dosage according to response. The dosage may be adjusted within the range of 5 mg three times daily to 20 mg three times daily.
Sublingual use of nifedipine in hypertensive crisis is not encouraged. In the case of pre-eclampsic toxemia, the capsule should be bitten open and the liquid contents held in the mouth.
Patients with hepatic dysfunction should commence therapy at 5 mg three times daily with careful monitoring. Patients with renal impairment should not require adjustment of dosage. There are no recommendations for use in children. Treatment may be continued indefinitely.
Lower doses may be required in elderly patients as a result of reduced drug clearance.
For hypertension, the dose used should not exceed 60 mg per day in divided doses.

Children : Dosage has not been established.

Shelf-life : 3 years from the date of manufacture.

Storage : Store below 25°C. Protect from light and moisture

Presentation/Packing : Soft capsule 10 mg x 30's, 100's in amber glass bottle.

Manufactured by : Hovid Sdn. Bhd., 121 Jalan Kuala Kangsar, 30010 Ipoh, Perak, Malaysia.