1.3 Product Information

1.3.1 Summary Product Characteristics (SPC):

Enclosed

1.3.1 Summary Product Characteristics

1. Name of the proprietary product:

Name of the nonproprietary International Product: NIFEDIPINE EXTENDED-RELEASE TABLETS USP 30 MG

Route of Administration: Oral

2. Qualitative and Quantitative

composition: Batch size: 100,000 Tablets

Sr. No	Name of Raw Material	Spec	Label claim / tab	Qty per tablet (mg)	% Overage	Std. Qty. (Kg)	Qty per tablet with Overages (kg)	Function
01	Nifedipine	USP	30 mg	30.00	-	3.000	3.00	Active
02	Maize Starch	BP	-	143.00	5%	14.300	15.015	Diluent
03	Lactose Monohydrate	BP	-	110.00	5%	11.000	11.550	Diluent
04	Microcrystalline cellulose	BP	-	110.00	-	11.000	11.000	Diluent
05	HPMC K100	BP	-	24.00	-	2.400	2.400	Disintegrate
06	Maize Starch	BP	-	5.000	-	0.500	0.500	Binder
07	P.V.P.K. 30	BP	-	3.000	-	0.300	0.300	Binder
08	Purified Water*	BP		q.s.	-	q.s.	q.s.	Binding Vehicle
09	Purified Talc	BP	-	3.000	-	0.300	0.300	Lubricant
10	Magnesium Stearate	BP	-	5.000	-	0.500	0.500	Lubricant
11	Sodium Starch Glycollate	BP	-	5.000	-	0.500	0.500	Disintegrate
12	Cross Carmelose Sodium	BP	-	8.000	-	0.800	0.800	Lubricant
13	Sodium Lauryl Sulphate	BP	-	2.000	-	0.200	0.200	Disintegrate
14	Colloidal Silicon Dioxide	BP	-	2.000	-	0.200	0.200	Disintegrate
15	Ready mix F/C powder yellow oxide of Iron	IHS	-	11.250	-	1.125	1.125	Colouring agent
16	Iso Propyl Alcohol*	BP	-	0.0001 mL	-	10.000	10.00	Solvent for coating solution preparation
	Avg. wt of tablet			**461.25 mg**		**46.125 kg**	**47.525 kg**	

3. Pharmaceutical Form:

A yellow coloured, Round Shaped, Biconvex Film coated tablet, plain on one side & other side embossed with ZMC"

4. Clinical Particulars:

4.1 Therapeutic indications

Management of chronic stable or vasospastic angina; treatment of hypertension.

4.2 Posology and method of administration

Adults: The recommended starting dose is 10 mg every 12 hours swallowed with water with subsequent titration of dosage according to response. The dose may be adjusted to40mg every 12 hours.

Children: Nifedipine ER tablets are not recommended for use in children.

Elderly: The pham1acokinetics of nifedipine is altered in the elderly so that lower maintenance doses of nifedipine may be required compared to younger patients.

Renal impairment: Dosage adjustments are not usually required in patients with renal impairment. Nifedipine Extended-Release Tablets should be swallowed whole and should not be bitten or divided.

4.3 Contraindications

Nifedipine ER tablets are contra-indicated in patients with known hypersensitivity to nifedipine or other dihydropyridines because of the theoretical risk of cross reactivity.

Nifedipine ER tablets should not be used in clinically significant aortic stenosis, unstable angina, or during or within one month of a myocardial infarction. They should not be used in patients in cardiogenic shock.

Nifedipine ER tablets should not be used for the treatment of acute attacks of angina, or in patients who have had ischaemic pain following its administration previously.

The safety of Nifedipine ER tablets in malignant hypertension has not been established.

Nifedipine ER tablets should not be used for secondary prevention of myocardial infarction.

Nifedipine ER tablets are contra-indicated in patients with acute porphyria.

Nifedipine ER tablets should not be administered concomitantly with rifampicin since effective plasma levels of nifedipine may not be achieved owing to enzyme induction.

4.4 Special warnings and precautions for use

Hypotension: Nifedipine should be used with caution in patients who are hypotensive; in patients with poor cardiac reserve; in patients with heart failure or significantly impaired left ventricular function as their condition may deteriorate; in diabetic patients as they may require adjustment of their diabetic therapy; and in dialysis patients with malignant hypertension and irreversible renal failure with hypovolaemia, since a significant drop in blood pressure may occur due to the vasodilator effects of nifedipine.

Peripheral Edema: It is a localized phenomenon thought to be associated with vasodilation of dependent arterioles and small blood vessels and not due to left ventricular dysfunction or generalized fluid retention. With patients whose angina or hypertension is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

Drive or use machinery: Excessive falls in blood pressure may result in transient blindness. If affected the patient should not attempt to drive or use machinery Gastrointestinal strictures: Alterations in gastrointestinal anatomy (e.g, severe gastrointestinal narrowing, history of GI cancer, obstruction, bowel resection, gastric bypass, vertical banded gastroplasty) and underlying hypomotility disorders have lead to bezoar formation with sustained release forms.

Hepatic impairment: Use with caution in patients with hepatic impairment. Clearance of nifedipine is reduced in cirrhotic patients leading to increased systemic exposure; monitor closely for adverse effects/toxicity and consider dose adjustments.

Pregnancy: Category C. Adverse events were observed in animal reproduction studies. Nifedipine crosses the placenta. Use in pregnancy only when clearly needed and when the benefits outweigh the potential hazard to the fetus.
Lactation: Nifedipine Extended release tablets are not recommended for use in lactating mothers as it excretes into breast milk.

4.5 Interaction with other medicinal products and other forms of interaction
Grape fruit juice: Nifedipine should not be taken with grapefruit juice because bioavailability is increased.
Beta-adrenergic blocking agents: Increase the likelihood of congestive heart fai lure, severe hypotension, or exacerbation of angina.
Digitalis: Administration of nifedipine with digoxin increased digoxin levels. Hence 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.
Alcohol, Alpha 1-Blockers, Antifungal Agents Cimetidine, Cisapride, Conivaptan, Cyclosporine (Systemic), Dasatinib, Fluconazole, H2-receptor antagonists Macrolide Antibiotics, Protease Inhibitors, Rifampicin, Antiepileptic: may increase the peak plasma concentration of Nifedipine.
Barbiturates, Deferasirox, Nafcillin: It may decrease the peak plasma concentration of Nifedipine.
Clopidogrel: Calcium Channel Blockers may diminish the therapeutic effect of Ciopidogrel Diazoxide, MAO Inhibitors, Prostacycin Analogues, Phosphodiesterase 5 Inhibitors, Pentoxifylline: May enhance the hypotensive effect of Nifedipine.

4.6 Fertility, pregnancy and lactation
Pregnancy: Category C. Adverse events were observed in animal reproduction studies. Nifedipine crosses the placenta. Use in pregnancy only when clearly needed and when the benefits outweigh the potential hazard to the fetus.
Lactation: Nifedipine Extended release tablets are not recommended for use in lactating mothers as it excretes into breast milk.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Common: Flushing, peripheral edema, dizziness, light headedness, giddiness, headache, Nausea, heartburn.
Rare: Palpitation, transient hypotension, CHF, nervousness, mood changes, fatigue, shakiness, jitteriness, sleep disturbances, difficulties in balance, fever, chills, dennatitis, pruritus, urticaria, sexual difficulties, diarrhea, constipation, cramps, flatulence, gingival hyperplasia, muscle cramps, tremor, weakness, inflammation, joint stiffness, blurred vision, cough, wheezing, nasal congestion, sore throat, chest congestion, dyspnea, diaphoresis.
Very rare: face edema, fever, hot flashes, malaise, periorbital edema, rigors, arrhythmia, hypotension, increased angina, tachycardia, syncope, anxiety, ataxia, decreased libido, depression, hypertonia, hypoesthesia, migraine, paroniria, tremor, vertigo, alopecia, increased sweating, urticaria, purpura, eructation, gastro esophageal reflux, gum hyperplasia, melena, vomiting, weight increase, back pain, gout, myalgias, upper respiratory tract infection, respiratory disorder, sinusitis, Abnormal lacrimation, abnormal vision, taste perversion, tinnitus, breast pain, dysuria, hematuria, nocturia.

4.9 Overdose
Experience with nifedipine over dosage is limited. Generally, over dosage with nifedipine 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 nifedipine would be expected to be prolonged in patients with impaired liver function. Since nifedipine is highly proteinbound, dialysis is not likely to be of any benefit.

5. Pharmacological Properties

5.1 Pharmacodynamics Properties

Calcium Channel Blocker, Anti-hypertensive and anti-anginal Inhibits calcium ion from entering the "slow channels" or select voltage-sensitive areas of vascular smooth muscle and myocardium during depolarization, producing a relaxation of coronary vascular smooth muscle and coronary vasodilation; increases myocardial oxygen delivery in patients with vasospastic angina; also reduces peripheral vascular resistance, producing a reduction in arterial blood pressure.

5.2 Pharmacokinetic Properties

Absorption: completely absorbed after oral administration. Plasma drug concentrations rise at a gradual, controlled rate after a Nifedipine Extended-Release tablet dose and reach a plateau at approximately six hours after the first dose. For subsequent doses, relatively constant plasma concentrations at this plateau are maintained with minimal fluctuations over the 24-hourdosing interval.
Distribution: Crosses placenta; enters breast milk
Protein binding(concentration dependent): 92% to 98%
Metabolism: Hepatic via CYP3A4 to inactive metabolites
Bioavailability: 65% to 89%; bioavailability increased with significant hepatic disease
Half-life Elimination: Adults: Healthy: 2-5 hours; Cirrhosis: 7 hours; Elderly: 7 hours Time to peak, serum: Extended release: 7 hours (range: 4-8 hours)
Excretion: Urine (60% to 80%as inactive metabolites); feces.

5.3 Preclinical Safety Data

Not Applicable

6 Pharmaceutical Particulars

6.1 List of Excipients

Maize Starch, Lactose Monohydrate, Microcrystalline cellulose, Hypromellose, Maize Starch, Povidone, Purified Water, Purified Talc, Magnesium Stearate, Sodium Starch Glycollate, Cross Carmelose Sodium, Sodium Lauryl Sulphate, Colloidal Anhydrous Silica, Ready mix F/C powder yellow oxide of Iron, Isopropyl Alcohol

6.2 Incompatibilities: Not Applicable

6.3 Shelf life: 36 months from the date of manufacturing.

6.4 Special precautions for storage

Do not store above 30°C, protect from light and moisture".

6.5 Nature and contents of container

Product available in 3 X 10 Tablets in Alu-Alu Blister pack.

6.6 Special precautions for disposal

No special requirements

6.7 Marketing Authorization Holder:

ZMC International Limited
7A Niger Street, Kano, Kano State Nigeria

6.8 Marketing Authorization Number:

6.9 Date of first Authorization /renewal of the authorization: ---

6.10 Date of revision of text: