1.6.1.1 Name of the medicinal Product

Nifedipine Sustained Release Tablets

1.6.1.1.1 strength

20 mg/tablet

1.6.1.1.2 Pharmaceutical Form

Oral tablet

1.6.1.2 Qualitative and Quantitative Composition

1.6.1.2.1 Qualitative declaration

Nifedipine BP

1.6.1.2.2 Quantitative declaration

Sr. No.	Ingredients	Specifications	Label Claim (mg/tablet)	Function
	Mixing:			
1	Nifedipine (A)	BP	20.00	Calcium Channel Blocker, Anti-hypertensive & Anti-anginal
2	Lactose Monohydrate (C)	BP	54.75	Diluent
3	Hypromellose (Metolose 90-SH-4000)	BP	16.00	Polymer
4	Maize Starch*	BP	11.56	Diluent
	Binding:			
5	Povidone (PVPK-90)	BP	5.00	Binder
6	Isopropyl Alcohol	BP	40.00	Binding Solvent
	Lubrication:			
7	Hypromellose (Metolose 90-SH-4000)	BP	9.00	Polymer
8	Purified Talc	BP	4.50	Anti-adherent
9	Colloidal Anhydrous Silica	BP	3.00	Glidant

10	Magnesium Stearate	BP	3.50	Lubricant
11	Sodium Starch Glycolate (Type-A)	BP	3.50	Surfactant
	Coating:			
12	Hypromellose BP (Methocel 15)	BP	2.20	Plasticizer
13	Titanium Dioxide	BP	0.33	Colouring agent
14	Colour Carmosine Supra	IH	0.13	Colouring agent
15	Colour Susnet Yellow Lake	IH	0.22	Colouring agent
16	Colour Indigo Carmine Lake	IH	0.17	Colouring agent
17	Diethyl Phthalate	BP	0.22	Solvent
18	Dichloromethane	BP	50.0	Solvent
19	Isopropyl Alcohol	BP	30.0	Solvent

1.6.1.3 Pharmaceutical Form

Semi Solid Dosage Form, Topical Cream

Purple coloured, round shaped, biconvex, film coated sustained release tablets, plain on both sides.

1.6.1.4 Clinical Particulars

1.6.1.4.1 Therapeutic Indications

Nifedipine Sustained Release Tablets are used in hypertension, in prophylaxis of angina pectoris particularly when a vasospastic element is present.

Use in Elders: Doses may need to be reduced in the elderly or those with impaired liver functions.

Use in Pregnancy: Nifedipine has been suggested for hypertension in pregnancy, if first line treatment with methyldopa or a beta-blocker failed to reduce blood pressure adequately. It has been tried in a limited numbers of patients with pre-eclampsia although it has been reported a high rate of caesarean delivaries, premature births & small-for-date infants in patients given nifedipine as a second line drug assessment of role of nifedipine is difficult because outcome is often poor in such severally compromised pregnancies.

1.6.1.4.2 Posology and Method of Administration

Nifedipine Sustained Release Tablets are normally given orally with or after food.

In the management of the hypertension, Nifedipine sustained release Tablets are given in the doses of 10-40 mg twice a daily, 30-90 mg once a daily, or 20-100 mg daily, depending on the preparation used.

In the management of angina pectoris, Nifedipine sustained release Tablets are given in the doses of 10-40 mg twice a daily or 30 to 90 mg once daily, depending on the preparation.

For Elderly Patients:

Nifedipine is normally given with or after food. Swallow tablet whole, do not bite, chew or divide. Dose of nifedipine may need to be reduced in the elderly and with impaired liver function. Titrate over a 7 to 14 days period starting with 30 mg once daily. Base upword titration on therapeutic efficacy & safety. Usual maintenance dose is 30 to 60 mg once daily. Titration dose more than 90 mg daily is not recommended. Closely monitor blood pressure since severe hypotension can occur.

1.6.1.4.3 Contraindications

Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. Peripheral oedema particularly in lower extremities can occur which responds to diuretic mother. No data are available regarding its use in lactation.

1.6.1.4.4 Special Warnings and Special Precautions for Use

Excessive Hypotension : Although in most patients the hypotensive effect of nifedipine is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension.

Increased Angina and/or Myocardial infarction : Rarely, patients, particularly those who have severe obstructive coronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial infarction upon starting nifedipine or at the time of dosage increase.

Beta-Blocker Withdrawal : When discontinuing a beta-blocker it is important to taper its dose, if possible, rather than stopping abruptly before beginning nifedipine.

Congestive Heart Failure: Rarely, patients (usually while receiving a beta-blocker) have developed heart failure after beginning nifedipine.

1.6.1.4.5 Interaction with other medicinal products and other forms of interaction

Increases digoxin blood levels. Concurrent use with beta-blockers leads to hypotension, angina and cardiac failure Synergism with Beta-blockers. Reverse depression of cardiac function caused by Beta-blockers. Cimetidine increase bioavailability and potentiates hypotensive action.

1.6.1.4.6 Fertility, Pregnancy and Lactation

Pregnancy: Nifedipine has been suggested for hypertension in pregnancy, if first line treatment with methyldopa or a beta-blocker failed to reduce blood pressure adequately. It has been tried in a limited numbers of patients with pre-eclampsia although it has been reported a high rate of caesarean delivaries, premature births & small-for-date infants in patients given nifedipine as a second line drug assessment of role of nifedipine is difficult because outcome is often poor in such severally compromised pregnancies.

1.6.1.4.7 Effects on ability To Drive and use Machines

Not Applicable

1.6.1.4.8 Undesirable Effects

The most common adverse effects are headache, flushing dizziness, gastrointestinal symptoms and lower leg oedema, swelling or fluid retention. The main vasodilator related adverse effects of NEPIN-SR tablet (headache, flushing and dizziness) have been reported to necessitate treatment withdrawal in 2-6% of patients.

1.6.1.4.9 Overdose

Experience with nifedipine overdosage is limited. Generally, overdosage with nifedipine leading to pronounced hypotension. The main effects of ingestion of approximately 4800 mg of nifedipine in a young man attempting suicide as a result of cocaine-induced depression was initial dizziness, palpitations, flushing, and nervousness. Within several hours of ingestion, nausea, vomiting, and generalized edema developed. Significant hyperglycemia was seen initially in this patient, but plasma glucose levels rapidly normalized without further treatment.

1.6.1.5 Pharmacological Properties

1.6.1.5.1 Pharmacodynamics Properties

Nifedipine is a calcium ion influx inhibitor (slow channel blocker or calcium ion antagonist) which inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The contractile processes of vascular smooth muscle and cardiac muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels. Nifedipine selectively inhibits calcium ion influx across the cell membrane of vascular smooth muscle and cardiac muscle without altering serum calcium concentrations. Nifedipine brings about an improvement in the oxygen supply to the heart muscle with simultaneous reduction of oxygen requirements, thereby exerting an antianginal effect. Normalization of elevated blood pressure is brought about by a reduction in peripheral resistance through the dilatation of the arterioles.

Mechanism of Action: The mechanism by which nifedipine reduces arterial blood pressure involves peripheral arterial vasodilatation and consequently, a reduction in peripheral vascular resistance. The increased peripheral vascular resistance that is an underlying cause of hypertension results from an increase in active tension in the vascular smooth muscle. Studies have demonstrated that the increase in active tension reflects an increase in cytosolic free calcium.

Nifedipine is a peripheral arterial vasodilator which acts directly on vascular smooth muscle. The binding of nifedipine to voltage-dependent and possibly receptor operated channels in vascular smooth muscle results in an inhibition of calcium influx through these channels. Stores of intracellular calcium in vascular smooth muscle are limited and thus dependent upon the influx of extracellular calcium for contraction to occur. The reduction in calcium influx by nifedipine causes arterial vasodilation and decreased peripheral vascular resistance which results in reduced arterial blood pressure.

1.6.1.5.2 Pharmacokinetic Properties

Nifedipine is completely absorbed after oral administration. The bioavailability of nifedipine as sustained release tablets relative to immediate release nifedipine is in the range of 84%-89%. After ingestion of Nifedipine Sustained Release Tablets under fasting conditions, plasma concentrations peak at about 2.5-5 hours with a second small peak or shoulder

evident at approximately 6-12 hours post dose. The elimination half-life of nifedipine administered as Sustained Release Tablets is approximately 7 hours in contrast to the known 2 hour elimination half-life of nifedipine administered as an immediate release capsule.

When Nifedipine Sustained Release Tablets is administered as multiples of 30 mg tablets over a dose range of 30 mg to 90 mg, the area under the curve (AUC) is dose proportional; however, the peak plasma concentration for the 90 mg dose given as 3 x 30 mg is 29% greater than predicted from the 30 mg and 60 mg doses.

Once daily dosing of Nifedipine Sustained Release Tablets under fasting conditions results in decreased fluctuations in the plasma concentration of nifedipine when compared to t. i. d. dosing with immediate release nifedipine capsules.

Nifedipine is extensively metabolized to highly water soluble, inactive metabolites accounting for 60% to 80% of the dose excreted in the urine. Only traces (less than 0.1% of the dose) of the unchanged form can be detected in the urine. The remainder is excreted in the feces in metabolized form, most likely as a result of biliary excretion. Because hepatic biotransformation is the predominant route for the disposition of nifedipine, its pharmacokinetics may be altered in patients with chronic liver disease. Nifedipine Sustained Release Tablet has not been studied in patients with hepatic disease; however, in patients with hepatic impairment (liver cirrhosis) nifedipine has a longer elimination half-life and higher bioavailability than in healthy volunteers. The degree of protein binding of nifedipine is high (92%-98%). Protein binding may be greatly reduced in patients with renal or hepatic impairment. After administration of Nifedipine Sustained Release Tablets to healthy elderly men and women (age 60 years), the mean Cm, is 36% higher and the average plasma concentration is 70% greater than in younger patients.

1.6.1.5.3 Preclinical Safety Data

Not Applicable.

1.6.1.6 Pharmaceutical Particulars

1.6.1.6.1 List of Excipients

Lactose Monohydrate BP

Hypromellose (Metolose 90-SH-4000) BP

Maize Starch BP

Povidone (PVPK-90) BP

Isopropyl Alcohol BP

Purified Talc BP

Colloidal Anhydrous Silica BP

Magnesium Stearate BP

Sodium Starch Glycolate (Type-A) BP

Hypromellose (Methocel 15) BP

Titanium Dioxide BP

Colour Carmosine Supra IHS

Colour Susnet Yellow Lake IHS

Colour Indigo Carmine Lake IHS

Diethyl Phthalate BP

Dichloromethane BP

1.6.1.6.2 Incompatibilities

Not applicable.

1.6.1.6.3 Shelf Life

36 months

1.6.1.6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light.

1.6.1.6.5 Nature and Contents of Container

Such 10 tablets are packed in blister pack. Such 10 blisters are packed in a printed carton with packing insert.

1.6.1.6.6 Special precaution for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

1.6.1.7 Marketing Authorization Holder and Manufacturing Site Addresses

1.6.1.7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.8 Marketing Authorization Number

To be included after obtaining first registration.

1.6.1.9 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

1.6.1.10 Date of Revision of the Text

January, 2023

1.6.1.11 Dosimetry (If Applicable)

Not Applicable

1.6.1.12 Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable