1. Name of the medicinal product
NIFESTAR SR (Nifedipine Sustain Release Tablets 20mg)

2. Qualitative and quantitative composition
Each film coated tablet contains 20 mg Nifedipine BP

Excipients of Known effects:
Refer to section 6.1 for the full list of excipients.

Excipients of known effect:
Each tablet contains 40.00mg of Lactose.

3. Pharmaceutical form
Tablet.
Yellow, round, Biconvex-shaped film- coated tablets plain on both sides.

4. Clinical Particulars:
4.1 Therapeutic indications
The tablets are indicated for:
- the treatment of all grades of hypertension
- the prophylaxis of chronic stable angina pectoris, either as monotherapy or in combination with a beta-blocker.

4.2 Posology and method of administration
These tablets should be swallowed whole with a glass of water and not bitten, broken up or chewed.
Nifedipine Sustain Release Tablets is particularly suitable for dose titration. Dose titration is recommended for hypertensives with severe cerebrovascular disease and for patients who, because of low body weight or multiple therapies with other antihypertensive drugs, are likely to have an excessive reaction to nifedipine. In addition, for patients who experience adverse effects in response to the nifedipine treatment, a finer dose adjustment is desirable and should be individually stabilized with **Nifedipine Sustain Release Tablets**.
Unless otherwise prescribed, the following dosage guidelines apply for adults:

In Coronary Heart Disease:	
Chronic stable angina pectoris	One **Nifedipine Sustain Release Tablets** twice daily
(angina of effort)	(2 x 20 mg/day)
If higher dosages are necessary, the dose can be increased in stages up to maximum 60 mg daily.	
In Hypertension:	One **Nifedipine Sustain Release Tablets** twice daily
	(2 x 20 mg/day)

Method of administration
Oral

4.3 Contraindications
Nifedipine Sustain Release Tablets should not be administered to patients with known hypersensitivity to the active substance, or to other dihydropyridines because of the theoretical risk of cross-reactivity, or to any of the excipients used in the formulation.
Nifedipine Sustain Release Tablets should not be used in cases of cardiogenic shock, clinically significant aortic stenosis, unstable angina, or during or within one month of a myocardial infarction.
Nifedipine Sustain Release Tablets should not be used for the treatment of acute attacks of angina.
The safety of Nifedipine Sustain Release Tablets in malignant hypertension has not been established.
Nifedipine Sustain Release Tablets should not be used for secondary prevention of myocardial infarction.
Owing to the duration of action of the formulation, Nifedipine Sustain Release Tablets should not be administered to patients with hepatic impairment.
Nifedipine Sustain Release Tablets should not be administered to patients with a history of gastro-intestinal obstruction, oesophageal obstruction, or any degree of decreased lumen diameter of the gastro-intestinal tract.
Nifedipine Sustain Release Tablets must not be used in patients with a Kock pouch (ileostomy after proctocolectomy).
Nifedipine Sustain Release Tablets is contra-indicated in patients with inflammatory bowel disease or Crohn's disease.
Nifedipine Sustain Release 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
Nifedipine Sustain Release Tablets must be swallowed whole; under no circumstances should they be bitten, chewed or broken up.
Caution should be exercised in patients with hypotension as there is a risk of further reduction in blood pressure and care must be exercised in patients with very low blood pressure (severe hypotension with systolic blood pressure less than 90 mm Hg).
Nifedipine Sustain Release Tablets should not be used during pregnancy unless the clinical condition of the woman requires treatment with nifedipine. Nifedipine Sustain Release Tablets should be reserved for women with severe hypertension who are unresponsive to standard therapy.
Careful monitoring of blood pressure must be exercised when administering nifedipine with I.V. magnesium sulfate, owing to the possibility of an excessive fall in blood pressure, which could harm both mother and foetus. For further information regarding use in pregnancy,

Nifedipine Sustain Release Tablets is not recommended for use during breast-feeding because nifedipine has been reported to be excreted in human milk and the effects of nifedipine exposure to the infant are not known.
In patients with impaired liver function careful monitoring and, in severe cases, a dose reduction may be necessary.
Nifedipine Sustain Release Tablets 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 Sustain Release Tablets will not prevent possible rebound effects after cessation of other antihypertensive therapy.
Nifedipine Sustain Release Tablets should be used with caution in patients whose cardiac reserve is poor. Deterioration of heart failure has occasionally been observed with nifedipine.
Diabetic patients taking Nifedipine Sustain Release Tablets may require adjustment of their control.
In dialysis patients with malignant hypertension and hypovolaemia, a marked decrease in blood pressure can occur.
Nifedipine is metabolised 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 or the clearance of nifedipine.
Drugs, which are known inhibitors of the cytochrome P450 3A4 system, and which may therefore lead to increased plasma concentrations of nifedipine include, for example:
- macrolide antibiotics (e.g., erythromycin)
- anti-HIV protease inhibitors (e.g., ritonavir)
- azole antimycotics (e.g., ketoconazole)
- the antidepressants, nefazodone and fluoxetine
- quinupristin/dalfopristin
- valproic acid
- cimetidine

Upon co-administration with these drugs, the blood pressure should be monitored and, if necessary, a reduction of the nifedipine dose should be considered.
As the outer membrane of the Nifedipine Sustain Release Tablets is not digested, what appears to be the complete tablet may be seen in the toilet or associated with the patient's stools. Also, as a result of this, care should be exercised when administering Nifedipine Sustain Release Tablets to patients, as obstructive symptoms may occur**.** Bezoars can occur in very rare cases and may require surgical intervention
In single cases, obstructive symptoms have been described without known history of gastrointestinal disorders.
A false positive effect may be experienced when performing a barium contrast x-ray.

4.5 Interaction with other medicinal products and other forms of interaction
Drugs that affect nifedipine
Nifedipine is metabolised 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 (after oral administration) or the clearance of nifedipine.
The extent as well as the duration of interactions should be taken into account when administering nifedipine together with the following drugs:
Rifampicin: Rifampicin strongly induces the cytochrome P450 3A4 system. Upon co-administration with rifampicin, the bioavailability of nifedipine is distinctly reduced and thus its efficacy weakened. The use of nifedipine in combination with rifampicin is therefore contraindicated.
Upon co-administration of known inhibitors of the cytochrome P450 3A4 system, the blood pressure should be monitored and, if necessary, a reduction in the nifedipine dose considered. In the majority of these cases, no formal studies to assess the potential for a drug interaction between nifedipine and the drug(s) listed have been undertaken, thus far.
Drugs increasing nifedipine exposure:
- macrolide antibiotics (e.g., erythromycin)
- anti-HIV protease inhibitors (e.g., ritonavir)
- azole anti-mycotics (e.g., ketoconazole)
- fluoxetine
- nefazodone
- quinupristin/dalfopristin
- cisapride
- valproic acid
- cimetidine
- diltiazem

Upon co-administration of inducers of the cytochrome P450 3A4 system, the clinical response to nifedipine should be monitored and, if necessary, an increase in the nifedipine dose considered. If the dose of nifedipine is increased during co-administration of both drugs, a reduction of the nifedipine dose should be considered when the treatment is discontinued.

Drugs decreasing nifedipine exposure:
- rifampicin (see above)
- phenytoin
- carbamazepine
- phenobarbital

Effects of nifedipine on other drugs
Nifedipine may increase the blood pressure lowering effect of concomitant applied antihypertensives.
When nifedipine is administered simultaneously with ß-receptor blockers the patient should be carefully monitored, since deterioration of heart failure is also known to develop in isolated cases.
Digoxin: The simultaneous administration of nifedipine and digoxin may lead to reduced digoxin clearance and, hence, an increase in the plasma digoxin level. The patient should therefore be subjected to precautionary checks for symptoms of digoxin overdosage and, if necessary, the glycoside dose should be reduced.

Quinidine: Co-administration of nifedipine with quinidine may lower plasma quinidine levels, and after discontinuation of nifedipine, a distinct increase in plasma quinidine levels may be observed in individual cases. Consequently, when nifedipine is either additionally administered or discontinued, monitoring of the quinidine plasma concentration, and if necessary, adjustment of the quinidine dose are recommended. Blood pressure should be carefully monitored and, if necessary, the dose of nifedipine should be decreased.
Tacrolimus: Tacrolimus is metabolised via the cytochrome P450 3A4 system. Published data indicate that the dose of tacrolimus administered simultaneously with nifedipine may be reduced in individual cases. Upon co-administration of both drugs, the tacrolimus plasma concentrations should be monitored and, if necessary, a reduction in the tacrolimus dose considered.
Drug food interactions
Grapefruit juice inhibits the cytochrome P450 3A4 system. Administration of nifedipine together with grapefruit juice thus results in elevated plasma concentrations and prolonged action of nifedipine due to a decreased first pass metabolism or reduced clearance. As a consequence, the blood pressure lowering effect of nifedipine may be increased. After regular intake of grapefruit juice, this effect may last for at least three days after the last ingestion of grapefruit juice. Ingestion of grapefruit/grapefruit juice is therefore to be avoided while taking nifedipine.
Other forms of interaction
Nifedipine may increase the spectrophotometric values of urinary vanillylmandelic acid, falsely. However, HPLC measurements are unaffected.
zinc sulfate reduce the absorption of tetracyclines.

4.6 Fertility, pregnancy and lactation
Pregnancy
Nifedipine should not be used during pregnancy unless the clinical condition of the woman requires treatment with nifedipine.
In animal studies, nifedipine has been shown to produce embryotoxicity, foetotoxicity and teratogenicity.
There are no adequate well controlled studies in pregnant women.
From the clinical evidence available a specific prenatal risk has not been identified, although an increase in perinatal asphyxia, caesarean delivery, as well as prematurity and intrauterine growth retardation have been reported. It is unclear whether these reports are due to the underlying hypertension, its treatment, or to a specific drug effect.
The available information is inadequate to rule out adverse drug effects on the unborn and newborn child. Therefore any use in pregnancy requires a very careful individual risk benefit assessment and should only be considered if all other treatment options are either not indicated or have failed to be efficacious.
Acute pulmonary oedema has been observed when calcium channel blockers, among others nifedipine, have been used as a tocolytic agent during pregnancy, especially in cases of multiple pregnancy (twins or more), with the intravenous route and/or concomitant use of beta-2 agonists.

Breast-feeding
Nifedipine is excreted in the breast milk. The nifedipine concentration in the milk is almost comparable with mother serum concentration. For immediate release formulations, it is proposed to delay breast-feeding or milk expression for 3 to 4 hours after drug administration to decrease the nifedipine exposure to the infant.
Fertility
In single cases of in vitro fertilisation calcium antagonists like nifedipine have been associated with reversible biochemical changes in the spermatozoa's head that may result in impaired sperm function. In those men who are repeatedly unsuccessful in fathering a child by in vitro fertilisation, and where no other explanation can be found, calcium antagonists like nifedipine should be considered as possible causes.

4.7 Effects on ability to drive and use machines
Reactions to nifedipine may vary in intensity in patients, especially at the onset of therapy, on changing medication or when combined with alcohol. Therefore, the patient should be warned of the possible effects advised not to drive or operate machinery, if affected.

4.8 Undesirable effects
Adverse drug reactions (ADRs) based on placebo-controlled studies with nifedipine sorted by CIOMS III categories of frequency (clinical trial data base: nifedipine n = 2,661; placebo n = 1,486; status: 22 Feb 2006 and the ACTION study: nifedipine n = 3,825; placebo n = 3,840) are listed below:
ADRs listed under "common" were observed with a frequency below 3% with the exception of oedema (9.9%) and headache (3.9%).
The frequencies of ADRs reported with nifedipine-containing products are summarised in the table below. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Frequencies are defined as common (≥1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100) and rare (≥ 1/10,000 to < 1/1,000). The ADRs identified only during the ongoing postmarketing surveillance, and for which a frequency could not be estimated, are listed under “Not known”.

System Organ Class (MedDRA)	**Common**	**Uncommon**	**Rare**	**Not Known**
Blood and Lymphatic System Disorders				Agranulocytosis Leucopenia
Immune System Disorders		Allergic reaction Allergic oedema/angioedema (incl. larynx oedema*)	Pruritus Urticaria Rash	Anaphylactic/ anaphylactoid reaction
Psychiatric Disorders		Anxiety reactions Sleep disorders		

Metabolism and Nutrition Disorders				Hyperglycaemia
Nervous System Disorders	Headache	Vertigo Migraine Dizziness Tremor	Par-/Dysaesthesia	Hypoaesthesia Somnolence
Eye Disorders		Visual disturbances		Eye pain
Cardiac Disorders		Tachycardia Palpitations		Chest pain (Angina pectoris)
Vascular Disorders	Oedema (incl. peripheral oedema) Vasodilatation	Hypotension Syncope		
Respiratory, Thoracic and Mediastinal Disorders		Nosebleed Nasal congestion		Dyspnoea Pulmonary oedema**
Gastrointestinal Disorders	Constipation	Gastrointestinal and abdominal pain Nausea Dyspepsia Flatulence Dry mouth	Gingival hyperplasia	Bezoar Dysphagia Intestinal obstruction Intestinal ulcer Vomiting Gastroesophageal sphincter insufficiency
Hepatobiliary Disorders		Transient increase in liver enzymes		Jaundice
Skin and Subcutaneous Tissue Disorders		Erythema		Toxic Epidermal Necrolysis Photosensitivity allergic reaction Palpable purpura
Musculoskeletal and Connective Tissue Disorders		Muscle cramps Joint swelling		Arthralgia Myalgia

Renal and Urinary Disorders		Polyuria Dysuria		
Reproductive System and Breast Disorders		Erectile dysfunction		
General Disorders and Administration Site Conditions	Feeling unwell	Unspecific pain Chills		

* = may result in life-threatening outcome
**cases have been reported when used as tocolytic during pregnancy.
In dialysis patients with malignant hypertension and hypovolaemia a distinct fall in blood pressure can occur as a result of vasodilation.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to National Regulatory Authority.

4.9 Overdose
Symptoms
The following symptoms are observed in cases of severe nifedipine intoxication:
Disturbances of consciousness to the point of coma, a drop in blood pressure, tachycardiac / bradycardiac heart rhythm disturbances, hyperglycaemia, metabolic acidosis, hypoxia, cardiogenic shock with pulmonary oedema.

Management
As far as treatment is concerned, elimination of nifedipine and the restoration of stable cardiovascular conditions have priority.
After oral ingestion thorough gastric lavage is indicated, if necessary in combination with irrigation of the small intestine.
Particularly in cases of intoxication with slow release nifedipine formulations, elimination must be as complete as possible, including the small intestine, to prevent the otherwise inevitable subsequent absorption of the active substance.
Haemodialysis serves no purpose as nifedipine is not dialysable, but plasmapheresis is advisable (high plasma protein binding, relatively low volume of distribution).
Hypotension as a result of cardiogenic shock and arterial vasodilatation can be treated with calcium (10-20 ml of a 10 % calcium gluconate solution administered slowly i.v. and repeated if necessary). As a result, the serum calcium can reach the upper normal range to slightly elevated levels. If an insufficient increase in blood pressure is achieved with calcium, vasoconstricting sympathomimetics such as

dopamine or noradrenaline should be administered. The dosage of these drugs should be determined by the patient's response.
Symptomatic bradycardia may be treated with atropine, beta-sympathomimetics or a temporary cardiac pacemaker, as required.
Additional liquid or volume must be administered with caution because of the danger of overloading the heart.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Selective calcium channel blockers with mainly vascular effect, dihydropyridine derivatives.
ATC code: C08CA05
Nifedipine is a specific and potent calcium antagonist of the 1,4-dihydropyridine type. Calcium antagonists reduce the transmembranal influx of calcium ion inflow through the slow calcium channel into the cell. Nifedipine acts particularly on the cells of the myocardium and the smooth muscle cells of the coronary arteries and the peripheral resistance vessels.
In hypertension, the main action of nifedipine is to cause peripheral vasodilatation and thus reduce peripheral resistance.
In angina, nifedipine reduces peripheral and coronary vascular resistance, leading to an increase in coronary blood flow, cardiac output and stroke volume, whilst decreasing after-load.
Additionally, nifedipine dilates submaximally both clear and atherosclerotic coronary arteries, thus protecting the heart against coronary artery spasm and improving perfusion to the ischaemic myocardium.
Nifedipine reduces the frequency of painful attacks and the ischaemic ECG changes irrespective of the relative contribution from coronary artery spasm or atherosclerosis.
Nifedipine administered twice-daily provides 24-hour control of raised blood pressure. Nifedipine causes reduction in blood pressure such that the percentage lowering is directly related to its initial level. In normotensive individuals, Nifedipine has little or no effect on blood pressure.
Paediatric population
Limited information on comparison of nifedipine with other antihypertensives is available for both acute hypertension and long-term hypertension with different formulations in different
dosages. Antihypertensive effects of nifedipine have been demonstrated but dose recommendations, long term safety and effect on cardiovascular outcome remain unestablished. Paediatric dosing forms are lacking.

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of single and repeated dose toxicity, genotoxicity and carcinogenic potential.
Following acute oral and intravenous administration of nifedipine in various animal species, the following LD_{50} (mg/kg) values were obtained:

Mouse:	Oral: 494 (421-572)*;	i.v.: 4.2 (3.8-4.6)*.
Rat:	Oral: 1022 (950-1087)*;	i.v.: 15.5 (13.7-17.5)*.
Rabbit	Oral: 250-500;	i.v.: 2-3.
Cat:	Oral: ~ 100;	i.v.: 0.5-8.
Dog:	Oral: > 250;	i.v.: 2-3.
		* 95% confidence interval.

In subacute and subchronic toxicity studies in rats and dogs, nifedipine was tolerated without damage at doses of up to 50 mg/kg (rats) and 100 mg/kg (dogs) p.o. over periods of thirteen and four weeks, respectively. Following intravenous administration, dogs tolerated up to 0.1 mg/kg nifedipine for six days without damage. Rats tolerated daily intravenous administration of 2.5 mg/kg nifedipine over a period of three weeks without damage.
In chronic toxicity studies in dogs with treatment lasting up to one year, nifedipine was tolerated without damage at doses up to and including 100 mg/kg p.o. In rats, toxic effects occurred at concentrations above 100 ppm in the feed (approximately 5-7 mg/kg bodyweight).
In a carcinogenicity study in rats (two years), there was no evidence of a carcinogenic effect of nifedipine.
Nifedipine has been shown to produce teratogenic findings in rats, mice and rabbits, including digital anomalies, malformation of the extremities, cleft palates, cleft sternum and malformation of the ribs.
Digital anomalies and malformation of the extremities are possibly a result of compromised uterine blood flow, but have also been observed in animals treated with nifedipine solely after the end of the organogenesis period.
Nifedipine administration was associated with a variety of embryotoxic, placentotoxic and foetotoxic effects, including stunted foetuses (rats, mice, rabbits), small placentas and underdeveloped chorionic villi (monkeys), embryonic and foetal deaths (rats, mice, rabbits) and prolonged pregnancy/decreased neonatal survival (rats; not evaluated in other species). The risk to humans cannot be ruled out if a sufficiently high systemic exposure is achieved, however, all of the doses associated with the teratogenic, embryotoxic or foetotoxic effects in animals were maternally toxic and were several times the recommended maximum dose for humans.
In in vitro and in vivo tests, nifedipine has not been associated with mutagenic properties.

6. Pharmaceutical particulars
6.1 List of excipients

Lactose
Maize Starch
Acrypol 912G
Iso propyl Alcohol

PVPK-30
Purified Talc
Magnesium Stearate
Colloidal Anhydrous Silica
Hydroxypropyl Methyl cellulose
Purified Water
Titanium Dioxide
Color Sunset Yellow
Mono propylene Glycol

6.2 Incompatibilities
None Known

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container
1 ALU-PVC Amber blister of 10 tablets, such 10 blisters packed in printed carton insert.

6.6 Special precautions for disposal and other handling
Not applicable.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER:

ZAIN PHARMA LTD.
Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa Road,
Behind Nice And Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. Marketing Authorization Number: CTD8894

9. Date of First Registration:

10. Date of Revision of the Text: 25/03/2026