PROFESSIONAL INFORMATION

FEDALOC SR RANGE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

FEDALOC 30 mg SR slow release film coated tablets

FEDALOC 60 mg SR slow release film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

FEDALOC 30 mg SR: Each slow release film coated tablet contains 30 mg nifedipine.

FEDALOC 60 mg SR: Each slow release film coated tablet contains 60 mg nifedipine.

Each FEDALOC 30 mg SR film coated tablet contains sugar (lactose monohydrate 15 mg).

Each FEDALOC 60 mg SR film coated tablet contains sugar (lactose monohydrate 30 mg).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Slow release film coated tablets.

FEDALOC 30 mg SR: Round, biconvex, pale red colour, marked "30" on one side and plain on the other side, film coated tablets in a slow release formulation. Diameter: 7,00 mm.

FEDALOC 60 mg SR: Round, biconvex, pale red colour, marked "60" on one side and plain on the other side, film coated tablets in a slow release formulation. Diameter: 11,00 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

FEDALOC SR is indicated for the

- treatment of mild to moderate hypertension
- prophylaxis and treatment of chronic stable angina pectoris.

4.2 Posology and method of administration

The recommended dosage is 30 mg (one tablet) once daily. This dosage may be increased according to individual requirements up to a maximum of 90 mg once daily.

In general, titration steps should proceed over a 7 to 14 day period so that the response to each dose level can be assessed before proceeding to higher doses.

Special populations

Patients with renal function impairment

Patients with impaired renal function should not require adjustment of dosage.

Elderly patients

A slight alteration of the pharmacokinetics of FEDALOC SR may be seen in the elderly. However, dosage adjustment in these patients is usually not necessary.

Patients with hepatic impairment

Owing to the duration of action of the formulation, FEDALOC SR should not be administered to patients with hepatic impairment.

Paediatric population

Safety and efficacy in children below the age of 18 years has not been established.

Method of administration

FEDALOC SR tablets should be swallowed whole with a glass of fluid. The tablets should not be divided, chewed or crushed. The tablets should be taken at approximately 24 hour intervals, i.e. at the same time each day, preferably in the morning.

FEDALOC SR may be taken with or without food.

Grapefruit juice should be avoided (see section 4.5).

Missed dose:

Doctors should advise patients who forget to take FEDALOC SR to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- hypersensitivity to nifedipine, other dihydropyridines or to any of the excipients of FEDALOC SR
- cardiogenic shock, unstable angina, myocardial infarction (acute with pulmonary congestion in the previous 4 weeks) or clinically significant aortic stenosis
- hepatic function impairment
- hypotension (severe hypotension with systolic pressure less than 90 mm Hg), in cases of manifest heart failure and in the case of severe aortic stenosis
- acute reduction of blood pressure in adults
- bradycardia
- heart failure
- FEDALOC SR should not be used for secondary prevention of myocardial infarction
- gastrointestinal obstruction (oesophageal obstruction or any decrease in the lumen diameter of the gastrointestinal tract)
- inflammatory bowel disease
- in combination with rifampicin due to enzyme induction by rifampicin, effective plasma levels of FEDALOC SR may not be obtained
- pregnancy and lactation (see section 4.6)
- treatment of acute attacks of angina, safety in malignant hypertension has not been established.
- patients with a Kock pouch (ileostomy after proctocolectomy).

4.4 Special warnings and precautions for use

Under no circumstances should FEDALOC SR be bitten, chewed or broken up. The tablets must be swallowed whole.

- FEDALOC SR should not be used in patients with hypotension, in patients whose cardiac reserve is poor, and in those with heart failure since deterioration of heart failure has been noted (see section 4.3).
- FEDALOC SR should not be used to treat an angina attack in chronic stable angina, nor should it be used for the acute reduction of blood pressure in adults (see section 4.3).
- In patients with severe aortic stenosis FEDALOC SR may increase the risk of developing heart failure (see section 4.3).
- FEDALOC SR should not be used during pregnancy (see sections 4.3 and 4.6).
- Careful monitoring of blood pressure must be exercised when administering FEDALOC SR with intravenous magnesium sulphate owing to the possibility of an excessive fall in blood pressure
- FEDALOC SR is not recommended for use during breastfeeding because nifedipine has been reported to be excreted in human milk and the effects of nifedipine exposure to the infant are not known (see sections 4.3 and 4.6).
- The dose may need to be reduced in patients with hepatic impairment (see section 4.3).
- FEDALOC SR may be used in combination with beta blocking medicines and other antihypertensive medicines but the possibility of an additive effect resulting in postural hypotension should be borne in mind. FEDALOC SR will not prevent possible rebound effects after cessation of other antihypertensive therapy.
- FEDALOC SR's effect on insulin and glucose responses may require antidiabetic therapy to be adjusted.
- In dialysis patients with malignant hypertension and hypovolaemia, a marked decrease in blood pressure can occur.
- FEDALOC SR is metabolised via the cytochrome P450 3A4 system. Medicines that are known to either inhibit or to induce this enzyme system may therefore alter the first pass or

the clearance of nifedipine (see section 4.5).

- Medicines, which are known inhibitors of the cytochrome P450 3A4 system, and which may therefore lead to increased plasma concentrations of nifedipine include, for example: (see section 4.5).
  - 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
  - diltiazem

    Upon co-administration with these medicines, the blood pressure should be monitored and, if necessary, a reduction of the nifedipine dose should be considered.
- Blood pressure should be monitored carefully during initiation and upward titration of FEDALOC SR tablets especially if patients are on other antihypertensive therapy.
- As the outer membrane of the FEDALOC SR tablet is not digested, what appears to be the complete tablet may be seen in the toilet or associated with the patient's stools. As a result of this, care should be exercised when administering FEDALOC SR to patients, as obstructive symptoms may occur. Bezoars may occur and may require surgical intervention.
- In single cases, obstructive symptoms have been described without known history of gastrointestinal disorders.
- FEDALOC SR is not a replacement for nitroglycerines in an acute attack of angina pectoris.
- Sudden withdrawal of FEDALOC SR might be associated with an exacerbation of angina.
- FEDALOC SR should be discontinued in patients who experience angina pectoris following its administration
- FEDALOC SR reduces the plasma aldosterone: renin ratio by increasing renin production and reducing plasma aldosterone concentrations. Consequently, primary

hyperaldosteronism has been misdiagnosed as essential hypertension

- A false positive effect may be experienced when performing a barium contrast x-ray
- Safety of nifedipine as tocolytic agent and in the treatment of hypertension in pregnancy after 20 weeks has not been established. Harm to the foetus cannot be excluded.
- Although a "steal" effect has not been demonstrated, FEDALOC SR therapy should be discontinued in patients experiencing this effect.
- The interchanging of slow release formulations of nifedipine, as in FEDALOC SR, is not advised.

Grapefruit and grapefruit juice

Administration of FEDALOC SR together with grapefruit juice results in elevated plasma concentrations of FEDALOC SR due to a decreased first pass metabolism in the gastrointestinal tract. The blood pressure lowering effect may therefore be increased.
This effect may last for at least 3 days after the last ingestion of grapefruit juice, upon regular intake.

FEDALOC SR may result in falsely elevated spectrophotometric values of urinary vanillyl-mandelic acid. However, measurement with HPLC is unaffected.

Quinidine

Concomitant use of quinidine and nifedipine, as in FEDALOC SR, is not recommended. When FEDALOC SR and quinidine are administered simultaneously, interactions may occur because it shares the same metabolic pathway. For this reason, when FEDALOC SR is either additionally administered or discontinued, monitoring of the quinidine plasma concentration and, if necessary, adjustment of the quinidine dose is recommended. The blood pressure should be carefully monitored if quinidine is added to an existing therapy with FEDALOC SR. If necessary, the dose of FEDALOC SR should be decreased, or FEDALOC SR should be discontinued.

Lactose

FEDALOC SR contains lactose. Patients with the rare hereditary conditions of galactose intolerance, e.g. galactosaemia, Lapp lactase deficiency or glucose-galactose malabsorption should not take FEDALOC SR.

FEDALOC SR contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

Medicines that affect nifedipine

Cytochrome P450 inhibitors or inducers

FEDALOC SR is metabolised via the cytochrome P450 3A4 system, located both in the intestinal mucosa and in the liver. The first pass (after oral administration) or clearance of FEDALOC SR may be altered by medicines that are known to either inhibit or to induce this enzyme system.

Rifampicin

Rifampicin is a strong inducer of the cytochrome P450 3A4 system. Co-administration with rifampicin, may reduce the bioavailability of nifedipine and its efficacy is therefore weakened. The use of FEDALOC SR in combination with rifampicin is therefore contraindicated.

Medicines increasing nifedipine exposure

Cimetidine

The use of FEDALOC SR with cimetidine may increase the bioavailability of nifedipine. Due to the inhibition of cytochrome P450 3A4 by cimetidine (and therefore inhibition of the metabolism of nifedipine), the antihypertensive effect may be potentiated.

Erythromycin

The macrolide antibiotics are inhibitors of cytochrome P450 isoenzyme CYP3A4 and may inhibit the metabolism of FEDALOC SR. The potential for an increase of FEDALOC SR plasma concentrations upon co- administration of both medicines cannot be excluded.

Indinavir, ritonavir, saquinavir

HIV-protease inhibitors are known to inhibit the cytochrome P450 isoenzyme CYP3A4 and may therefore interfere with the metabolism of FEDALOC SR. When administered together with FEDALOC SR, a substantial increase in plasma concentrations of FEDALOC SR due to a decreased first pass metabolism and a decreased elimination cannot be excluded. Blood pressure should be monitored and if necessary, a reduction or discontinuation in the FEDALOC SR dose considered.

Ketoconazole, itraconazole, fluconazole

Azole antifungals inhibit the cytochrome P450 enzyme system and may therefore interfere with the metabolism of FEDALOC SR. If these antifungals are administered together with FEDALOC SR, an increase in system bioavailability of FEDALOC SR may occur due to a decreased first pass hepatic metabolism.

Blood pressure should be monitored and, if necessary, a reduction in the FEDALOC SR dose considered.

Nefazodone

Nefazodone is known to inhibit cytochrome P450 3A4 mediated metabolism of other medicines. An increase of nifedipine plasma concentrations may occur when these medicines are given together. If these medicines are given together, the blood pressure should be monitored and the FEDALOC SR dose may be adjusted if necessary.

Quinupristin/Dalfopristin

Increased plasma concentrations of nifedipine may develop after concomitant administration of quinupristin/dalfopristin and FEDALOC SR. When both medicines are used together, the blood pressure should be monitored and if necessary a reduction of the FEDALOC SR dose considered.

Diltiazem

Plasma concentrations of nifedipine may be increased and the clearance decreased when used in combination with diltiazem. FEDALOC SR increases the bioavailability and decreases the clearance of diltiazem. The combination of both medicines should be administered with caution and a reduction of both doses may be considered.

Cisapride

Increased plasma concentration of FEDALOC SR may develop when using cisapride simultaneously with FEDALOC SR. When using both medicines together, the blood pressure should be monitored and if necessary, a reduction of the FEDALOC SR dose considered.

Fluoxetine

Fluoxetine may inhibit the metabolism of FEDALOC SR resulting in an increase of nifedipine plasma concentrations. If fluoxetine is given in combination with FEDALOC SR, the blood pressure should be monitored and a reduction in the FEDALOC SR dose may be necessary.

Valproic acid

Valproic acid has been reported to increase plasma nimodipine concentrations and therefore an increase in FEDALOC SR plasma concentrations cannot be excluded.

Medicines decreasing nifedipine exposure

Rifampicin

See above.

Phenytoin

The effects of nifedipine may be reduced by enzyme-inducing antiepileptics such as phenytoin, which induces the cytochrome P450 3A4 system. Concomitant use of phenytoin and FEDALOC SR results in a reduced bioavailability of nifedipine. The clinical response to FEDALOC SR should be monitored and, if necessary, an increase of the FEDALOC SR dose considered. If the dose of FEDALOC SR is increased during co-administration of both medicines, a reduction of the FEDALOC SR dose should be considered when the treatment with phenytoin is discontinued.

Carbamazepine

The effect of FEDALOC SR may be reduced by enzyme-inducing antiepileptics such as carbamazepine.

Phenobarbitone

Enzyme-inducing antiepileptics such as phenobarbitone may reduce the effect of FEDALOC SR.

Effects of nifedipine on other medicines

Nifedipine, as in FEDALOC SR, may exacerbate the blood pressure lowering effect of concomitant applied antihypertensives such as diuretics, β-blockers, ACE-inhibitors, angiotensin receptor blockers, other calcium channel blockers, α-adrenergic blocking medicines, PDE5 inhibitors and α-methyldopa.

Antihypertensives

Nifedipine, as in FEDALOC SR, may enhance the antihypertensive effect of other antihypertensive medicines. Severe hypotension may occur when FEDALOC SR is administered simultaneously with ß-receptor blockers. The patient should be carefully monitored. Deterioration of heart failure is also known to develop (see section 4.3).

Digoxin

Concurrent use of digoxin with FEDALOC SR may increase serum concentration of digoxin. The patient should therefore be monitored for symptoms of digoxin overdosage as a precaution and, if necessary, the digoxin dose should be reduced taking account of the plasma concentration of digoxin.

Quinidine

Concomitant use of quinidine and nifedipine, as in FEDALOC SR, is not recommended (see section 4.4). When FEDALOC SR and quinidine are administered simultaneously, interactions may occur because it shares the same metabolic pathway. For this reason, when FEDALOC SR is either additionally administered or discontinued, monitoring of the quinidine plasma concentration and, if necessary, adjustment of the quinidine dose is recommended.

The blood pressure should be carefully monitored if quinidine is added to an existing therapy with FEDALOC SR. If necessary, the dose of FEDALOC SR should be decreased, or FEDALOC SR should be discontinued.

Tacrolimus

Tacrolimus has been shown to be metabolised via the cytochrome P450 3A4 system. Concomitant use of FEDALOC SR with tacrolimus may increase blood concentration of tacrolimus. Tacrolimus

concentration should be monitored, and if necessary, a reduction in the tacrolimus dose considered.

FEDALOC SR-food interactions

Grapefruit or grapefruit juice

Administration of FEDALOC SR together with grapefruit juice results in elevated plasma concentrations of FEDALOC SR due to a decreased first pass metabolism in the gastrointestinal tract. The blood pressure lowering effect may therefore be increased. This effect may last for at least 3 days after the last ingestion of grapefruit juice, upon regular intake (see section 4.4).

Other forms of interaction

Nifedipine may increase the spectrophotometric values of urinary vanillylmandelic acid, falsely. However, HPLC measurements are unaffected.

Tobacco

Cigarette smoking has been shown to have direct and adverse effects on the heart and to interfere with the efficacy of nifedipine.

Valproic acid

Valproic acid has been reported to increase plasma nimodipine concentrations and therefore an increase in FEDALOC SR plasma concentrations cannot be excluded.

Alcohol

Alcohol may inhibit the metabolism of FEDLOC SR.

4.6 Fertility, pregnancy and lactation

Pregnancy

FEDALOC SR tablets should not be used during pregnancy (see section 4.3).

In animal studies, nifedipine has been shown to produce embryotoxicity, foetotoxicity and teratogenicity. There are no adequate and 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 medicine effect.

The available information is inadequate to rule out adverse medicine effects on the unborn and newborn child.

Co-administration of nifedipine with intravenous magnesium sulphate may cause an excessive fall in blood pressure which could harm both mother and foetus.

Breastfeeding

FEDALOC SR tablets should not be used during breastfeeding (see section 4.3).

Nifedipine is excreted in the breast milk. Mothers taking FEDALOC SR should not breastfeed their infants.

Fertility

FEDALOC SR has been associated with reversible biochemical changes in the spermatozoa's head section in *in vitro* fertilisation and may result in impaired sperm function. In men who are repeatedly unsuccessful in *in vitro* fertilisation and if no other explanation can be found, FEDALOC SR should be considered a possible reason.

4.7 Effects on ability to drive and use machines

FEDALOC SR may impair the ability to drive or use machines. This applies particularly at the start of treatment, on changing the medication and in combination with alcohol. Patients are advised to take special care before performing tasks requiring their attention, until they know how FEDALOC SR will affect them.

4.8 Undesirable effects

Tabulated list of adverse reactions

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	Less frequent Frequency unknown	Haemorrhagic complications in surgical patients, blood dyscrasias Agranulocytosis, leucopenia
Immune system disorders	Less frequent Frequency unknown	Hypersensitivity reactions: rash, erythema multiforme, allergic oedema / angioedema (incl. larynx oedema*), pruritus, urticaria Anaphylactic/anaphylactoid reaction
Metabolism and nutrition disorders	Frequency unknown	Hyperglycaemia
Psychiatric disorders	Less frequent	Insomnia, hyper excitability, pacing, agitation, mental depression, mood disorders, anxiety reactions, sleep disorders
Nervous system disorders	Frequent Less frequent Frequency unknown	Headache, light-headedness Dizziness, migraine, tremor, paraesthesia, dysaesthesia, somnolence, lethargy, cerebral ischaemia Hypoaesthesia
Eye disorders	Frequent Less frequent	Eye pain Visual disturbances, stinging, transient blindness, transient retinal ischaemia, amblyopia
Ear and labyrinth disorders	Less frequent	Tinnitus, vertigo
Cardiac disorders	Less frequent	Palpitations, tachycardia, chest pain (angina pectoris), complete heart block, sudden circulatory collapse
Vascular disorders	Frequent Less frequent	Oedema (incl. peripheral oedema), vasodilatation Syncope, flushing, hypotension

Respiratory, thoracic and mediastinal disorders	Less frequent Frequency unknown	Nasal congestion, nosebleed, distortion of smell Dyspnoea, reversible acute pulmonary oedema**
Gastrointestinal disorders	Frequent Less frequent Frequency unknown	Constipation Gastrointestinal disturbances – gingival hyperplasia, nausea, gastrointestinal and abdominal pain, nausea, dyspepsia, flatulence, dry mouth, gastroesophageal sphincter insufficiency Bezoar, dysphagia, intestinal obstruction, vomiting, intestinal ulcer
Hepatobiliary disorders	Less frequent Frequency unknown	Abnormalities in liver function, transient increase in liver enzymes, hepatitis, cholestasis Jaundice
Skin and subcutaneous tissue disorders	Frequent Less frequent Frequency unknown	Skin rashes, pruritus, urticaria, alopecia, exfoliative dermatitis Erythema multiforme, Stevens Johnson's syndrome, non-thrombocytopenic purpuric rash, telangiectasias, photo- distributed telangiectasias, pemigold nodularis, palpable purpura Toxic epidermal necrolysis, photosensitivity reactions
Musculoskeletal, connective tissue and bone disorders	Less frequent	Muscle cramps, joint swelling, arthralgia, myalgia
Renal and urinary disorders	Less frequent	Increased micturition frequency, polyuria, dysuria, diuresis, nocturia
Pregnancy, puerperium and perinatal conditions	Less frequent	Erectile dysfunction, gynecomastia, menorrhagia, menstrual irregularity with heavy bleeding

General disorders and administrative site conditions	Frequent Less frequent	Feeling unwell Unspecific pain, chills

* may result in life-threatening outcome

In dialysis patients with malignant hypertension and hypovolaemia a distinct fall in blood pressure can occur as a result of vasodilation.

**cases have been reported when used as tocolytic during pregnancy (see section 4.6).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8 or http://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

Disturbances of consciousness to the point of coma, a severe drop in blood pressure, tachycardia, bradycardia, hyperglycaemia, metabolic acidosis, hypoxia, cardiogenic shock with pulmonary oedema, flushing, headaches.

Management of overdose:

No specific antidote is available. Treatment is symptomatic and supportive.

As far as treatment is concerned, particularly in cases of intoxication with slow release products like FEDALOC SR, elimination of nifedipine and the restoration of stable cardiovascular conditions have priority. Elimination must be as complete as possible, including the small intestine, to prevent the otherwise inevitable subsequent absorption of the active substance.

Consider activated charcoal (50 g for adults, 1 g/kg for children) if the patient presents within 1 hour of ingestion of a potentially toxic amount. Although it may seem reasonable to assume that late administration of activated charcoal may be beneficial for sustained release (SR, MR) preparations, there is no evidence to support this.

Consider further doses of activated charcoal every 4 hours if a clinically significant amount of a sustained release preparation has been ingested with a single dose of an osmotic laxative (e.g. sorbitol, lactulose or magnesium sulphate).

Asymptomatic patients should be observed for at least 4 hours after ingestion and for 12 hours if a sustained release preparation has been taken.

Nifedipine does not appear to be removed by haemodialysis or chronic ambulatory peritoneal dialysis, however, plasmapheresis may be beneficial.

Symptomatic bradycardia may be treated with atropine, ß-sympathomimetics and in life-threatening bradycardiac disturbances of heart rhythm, temporary cardiac pacemaker therapy is advisable.

Hypotension as a result of cardiogenic shock and arterial vasodilation may be treated with calcium (10 - 20 mL of a 10 % calcium gluconate solution administered slowly intravenously and repeated if necessary). As a result, the serum calcium may reach the upper normal to slightly elevated levels.

If an insufficient increase in blood pressure is achieved with calcium, vasoconstricting sympathomimetics, such as dopamine or norepinephrine (noradrenaline), may be administered additionally.

The dosage of these medicines is determined solely by the effect obtained.

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

Pharmacological classification: Vasodilators, hypotensive medicines.

Mechanism of action

Nifedipine is a dihydropyridine calcium channel blocker. It inhibits the voltage-dependent calcium channels in vascular smooth muscle at significantly lower concentrations than is required to interfere with the release of intracellular calcium to block receptor operated calcium channels. By reducing the intracellular calcium concentration in cardiac and vascular smooth muscles, it dilates coronary arteries, peripheral arteries and arterioles. Nifedipine results primarily in vasodilatation, with reduced peripheral resistance, blood pressure and afterload. It may reduce heart rate, decrease myocardial contractility (negative inotropic effect) and slow atrioventricular (AV) nodal conduction. This results in an increase in myocardial oxygen supply and cardiac output. Nifedipine has no antidysrhythmic activity.

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.

5.2 Pharmacokinetic properties

General characteristics

Nifedipine slow release tablets are formulated to provide nifedipine at an approximately constant rate over 24 hours. Nifedipine is released from the tablet at a zero-order rate by a membrane

controlled, osmotic push-pull process. The pharmacokinetic profile of this formulation is characterized by low peak-trough fluctuation. 0 - 24 hour plasma concentration versus time profiles at steady state are plateau-like, rendering the nifedipine slow release tablets appropriate for once-a-day administration.

The delivery rate is independent of gastrointestinal pH or motility. Upon swallowing, the biologically inert components of the tablet remain intact during gastrointestinal transit and are eliminated in the faeces as an insoluble shell.

Absorption:

Nifedipine is well absorbed from the gastrointestinal tract. After oral administration, bioavailability is reduced to between 60 and 75 % due to first-pass hepatic metabolism. Peak blood concentrations may occur approximately 6 hours after oral administration of nifedipine slow release tablets. Administration in the presence of food slightly alters the early rate of absorption but does not influence the extent of nifedipine availability.

Distribution:

Nifedipine is bound to plasma proteins to a significant extent (92 to 98 %). The distribution half-life after intravenous administration has

been determined to be 5 to 6 minutes.

Biotransformation:

After oral administration, nifedipine is metabolised in the gut wall and in the liver, primarily by oxidative processes. These metabolites show no pharmacodynamic activity.

After hepatic metabolism, approximately 70 to 80 % of a dose is excreted in the urine (below 0,1 %) and about 5 – 15 % via the bile in the faeces, almost entirely as inactive metabolites.

Elimination:

The terminal elimination half-life is 1,7 to 3,4 h in conventional formulations. The terminal half-life following slow release tablet administration does not represent a meaningful parameter as a plateau-like plasma concentration is maintained during release from the tablets and absorption.

After release and absorption of the last dose the plasma concentration finally declines with an elimination half-life as seen in conventional formulations.

Pharmacokinetics in special patient groups

Renal impairment

There are no significant differences in the pharmacokinetics of nifedipine between healthy subjects and subjects with renal impairment. Therefore, dosage adjustment is not needed in these patients

Hepatic impairment

The elimination half-life is distinctly prolonged and the total clearance is reduced. Owing to the duration of action of the formulation, nifedipine slow release tablets should not be administered in these patients.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet cores

Carbomer

Hydroxypropylmethylcellulose

Lactose monohydrate

Magnesium stearate

Povidone K30

Silica colloidal anhydrous

Talc

Film coating

Eudragit E

Ferric oxide red (77491)

Hydroxypropylmethylcellulose

Macrogol 4000

Magnesium stearate

Talc

Titanium dioxide (77891)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light and moisture.

Keep the blister in the outer carton until required for use.

Keep the container well closed.

6.5 Nature and contents of container

White polypropylene securitainers with white polyethylene tear tab caps and foam insert containing 30 or 100 tablets.

Opaque white, PVC/PVDC/ Aluminium foil blisters containing 28 tablets in an outer carton.

Opaque white, PVC/PVDC/ Aluminium foil blisters containing 30 tablets in an outer carton.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor Grapevine House,

Steenberg Office Park

Silverwood Close

Westlake

Cape Town,7945

South Africa

8. REGISTRATION NUMBER(S)

FEDALOC 30 mg SR: A37/7.1/0302

FEDALOC 60 mg SR: A37/7.1/0303

9. DATE OF FIRST AUTHORISATION

FEDALOC 30 mg SR: 15 August 2008

FEDALOC 60 mg SR: 15 August 2008

10. DATE OF REVISION OF THE TEXT

01 March 2023

NAMIBIA:

FEDALOC SR 30 mg: NS2 10/7.1/0033

FEDALOC SR 60 mg: NS2 10/7.1/0034

MOZAMBIQUE

FEDALOC 30 mg SR: 4323

FEDALOC 60 mg SR: 4324