Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nifedipine 10 mg STADA Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 10 mg Nifedipine.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Soft capsule.

Brown capsule, oblong, content consists of a yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

(i) Chronic stable angina.

(ii) mild to moderate hypertension.

4.2 Posology and method of adminstration

4.2.1 Dosage

Adults / Elderly:

The recommended dose is 5 to 10 mg three times a day. The maximum daily dose should not exceed 20 mg three times a day. Patients with hepatic dysfunction should commence therapy at 5 mg three times a day. No dosage adjustment is normally required in patients with renal dysfunction.

Therapy may be indefinitely continued.

Children:

Not recommended.

4.2.2 Administration

For oral administration only.

4.3 Contraindications

Use in patients hypersensitive to the active ingredient.

Use in patients with cardiogenic shock.

Unstable angina pectoris.

Acute myocardial infarction (within the first 4 weeks).

Use in women capable of child-bearing or to nursing mothers.

4.4 Special warnings and special precautions for use

The use of nifedipine in diabetic patients may require adjustment of their control.

Nifedipine should be used with caution in patients with poor cardiac reserve or severe hypotension. Deterioration of heart failure has occasionally been observed with nifedipine.

The introduction of nifedipine therapy may induce attacks of ischaemic pain in some patients with angina pectoris commonly within 30 minutes of taking nifedipine. Should this occur treatment should be stopped.

Patients should be advised that nifedipine may modify patients performance at skilled tasks (driving, operating machinery, etc.) to a varying degree depending upon dosage and individual susceptibility.

Treatment with short acting nifedipine may induce an abrupt fall in blood pressure as well as tachycardia, which could lead to a detrimental outcome.

There is some concern about increased mortality and morbidity in the treatment of ischaemic heart disease, especially at higher dosages. Treatment with short-acting nifedipine may exacerbate angina pectoris. There is no evidence that short-acting nifedipine confers benefit in secondary prevention of myocardial infarction.

4.5 Interaction with other medicinal products and other forms of interaction

The antihypertensive effect of nifedipine may be potentiated by other antihypertensive drugs and tricyclic antidepressants.

Use of nifedipine may be combined with diuretics and beta-adrenoceptor blockers in antihypertensive therapy.

However, introduction of such concurrent treatment should be conducted with care, as a major lowering of blood pressure may be produced. Nifedipine will not protect against the effects of withdrawal of beta-adrenoceptor blocking agents, nor the rebound effects seen with various antihypertensives.

Any such withdrawal should be a gradual reduction of the dose of beta-blockers over 8 to 10 days.

In combined therapy with quinidine, the quinidine plasma level must be monitored, as nifedipine can cause a marked increase in quinidine plasma levels.

Nifedipine may cause an increase in the plasma levels of digoxin or theophylline; control of the latter is recommended.

Cimetidine, and to a lesser extent, ranitidine, may lead to an increase in the nifedipine plasma level. Diltiazem decreases the clearance of nifedipine and therefore increases plasma nifedipine levels. Both drugs should be used together with caution and a reduction of the nifedipine dose may be necessary.

As with other dihydropyridines, nifedipine should not be taken with grapefruit juice because bioavailability is increased.

4.6 Pregnancy and lactation

Nifedipine should not be administered to women capable of childbearing. Nifedipine must not be administered to pregnant women as foetal abnormalities have been observed in experimental (animal) studies. No data is available in

humans.

Nifedipine has been detected in breast milk. If treatment is essential, an alternative method of feeding should be instituted.

4.7 Effects on ability to drive and use machines

The occurrence of reactions, which may differ in severity from one person to another, may impair the patient's ability to drive vehicles and to operate machinery. This precaution applies particularly at the beginning of therapy, or when dosage is changed, or with concurrent consumption of alcohol.

4.8 Undesirable effects

Most side-effects are due to the hypotensive action of nifedipine. Especially at the beginning of treatment, headaches, flushing, and a sensation of warmth have been reported.

Occasionally, tachycardia, palpitations, lower leg oedema (due to vasodilatation), fatigue or vertigo may occur. Also occasionally, paraesthesia and a drop in blood pressure.

In rare cases, nausea, diarrhoea, allergic reactions and in individual cases photosensitivity and exfoliative dermatitis have been reported. Also micturition difficulties, impotence or tremors. Other less frequent reported side-effects include myalgia, tremor and visual disturbances.

In individual cases, an increase in the blood sugar level in the serum (hyperglycaemia) has been observed. This should be taken into account in patients suffering from diabetes mellitus.

Very rarely, on long term treatment, gingival hyperplasia has been reported as well as a few cases of liver dysfunctions (intrahepatic cholestasis, increases in transaminases) or hypersensitivity type jaundice.

These reactions normally regress on discontinuing therapy.

4.9 Overdose

Symptoms: Flushing, headache, increased heart rate, hypotension.

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 for treatment of hypotension, with intravenous atropine and/or beta-sympathomimetics for bradycardia.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Nifedipine is a vasodilator slow calcium channel antagonist. Its main action is to relax arterial smooth muscle in the coronary and peripheral circulation.

5.2 Pharmacokinetic properties

Nifedipine is well absorbed with an elimination half life of 2 to 5 hours. Systemic bioavailability is 50 - 70 % due to first-pass metabolism. Peak plasma concentrations are reached after 15 to 75 minutes for the immediate release formulations and 2 to 5 hours for the modified release preparation.

Its hypotensive effect extends to 6 to 8 hours maximum for the immediate release formulations and 10 to 12 hours maximum for the modified release preparation.

The drug is metabolised to inactive substances and excreted mostly via the kidney. The drug is strongly protein bound (approx. 95%).

5.3 Preclinical safety data

Acute toxicity and chronic toxicity studies have been carried out on various animal studies. No toxic effects were observed. No tumorigenic or mutagenic potential has been noted. However, teratogenic effects were observed in studies on three species of animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin
Glycerol
Saccharin sodium
Macrogol 400
Racementhol
Purified water
Titanium dioxide (E171)
Ferric oxide black (E172)
Ferric oxide yellow (E172)
Ferric oxide red (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original container.

6.5 Nature and contents of container

Al/PVC/PVDC blister packs in a cardboard outer container. Pack sizes 20, 50, 100.

6.6 Instructions for use and handling

None.

7 MARKETING AUTHORISATION HOLDER

Stada Arzneimittel AG
Stadastraβe 2-18,
61118 Bad Vilbel,

Germany

8 MARKETING AUTHORISATION NUMBER

PA 593/3/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th April 1997
Date of last renewal: 4th April 2002

10 DATE OF REVISION OF THE TEXT

June 2002