1.3.1
Summary Of Product Characteristics (SPC)

1.3.1 Summary of Product Characteristics

1.3.1.1 Invented Name of the Medicinal Product

AFADOPINE 5

Amlodipine Besylate Tablets USP 5 mg

1.3.1.2 Strength

Amlodipine Besylate Tablets USP 5 mg

1.3.1.3 Dosage Form

Solid Dosage Form

1.3.1.4 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Amlodipine Besylate USP

Eq. to Amlodipine……..5 mg.

Excipients……..……..…....Q.S.

1.3.1.5 PHARMACEUTICAL FORM

Uncoated Tablets.

White colour round shaped biconvex uncoated tablet, plain on both sides.

1.3.1.6. CLINICAL PARTICULARS

1.3.1.6.1 Therapeutic indications

AFADOPINE 5 is indicated for the first line treatment of hypertension and can be used as a sole agent to control blood pressure in the majority of patients. Patients not adequately controlled on a single antihypertensive agent may benefit from the addition of amlodipine, which has been used in combination with thiazide diuretic, diuretic, alpha blockers, and beta adrenoceptor blocking agent or an angiotensin converting enzyme inhibitor.

AFADOPINE 5 is indicated for the first line treatment of myocardial ischemia, whether due to fixed obstruction (stable angina) or/vasospasm/vasoconstriction (Prinzmelal's or variant angina) of coronary vasculature.

AFADOPINE 5 may be used where the clinical presentation suggests a possible vasospastic/vasoconstrictive component but where vasospasm/vasoconstriction has not been confirmed. RELODIPINmay be used alone as monolherapy or in combination with other antianginal drugs in patients with angina that is refractory lo nitrates and/or adequate doses of beta-blockers.

1.3.1.6.2 POSOLOGY AND METHOD OF ADMINISTRATION

For both hypertension and angina, the usual initial dose is 5mg AFADOPINE 5 once daily, Which may be increased to a maximum dose of 10mg depending on the individual patient's response.

No dose adjustment of AFADOPINE 5 is required upon concomitant administration of Lhiazide diuretic, beta blockers, and angiolensin converting enzyme (ACE) inhibitors.

Use in the Elderly

Normal dosage regimens are recommended, similar dosage of AFADOPINE 5 is well tolerated in both elderly and young patients.

Use in children

Safety and effectiveness of amlodipine in children have not been established.

Use in Patients with impaired Hepatic function

As with all calcium antagonists, amlodipine's half-life is prolonged in patients with impaired liver function and dosage recommendations have not been established. The drug should therefore be administered with caution in these patients.

Use in Renal Failure

AFADOPINE 5 may be used in such patients at normal doses. Changes in AFADOPINE 5 plasma concentrations are correlated with degree of renal impairment. AFADOPINE 5 is not dialyzable.

1.3.1.6.3 CONTRAINDICATIONS

AFADOPINE 5 is contraindicated in-patients with a known sensitivity lo dihydropyridines, amlodipine or any of the inert ingredients.

1.3.1.6.4 WARNING AND PRECAUTIONS

Use in patients with impaired hepatic function

As with all calcium antagonists, AFADOPINE 5 half-life is prolonged in patients with impaired liver function and dosage recommendations have not been established. The drug should therefore be administered with caution in these patients.

1.3.1.6.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

AFADOPINE 5 has been safely administered with thiazide diuretics, alpha blockers, beta-blockers, angiotensin-converting enzyme inhibitors, long acting nitrates, sublingual nitroglycerin, non-steroidal anti-inflammatory drugs, antibiotics and oral hypoglycemic drugs. Special studies have indicated that the co-administration of AFADOPINE 5 with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers and that co-administration of cimetidine did not alter the pharmacokinetics of amlodipine.

In vitro data from human plasma studies indicate that AFADOPINE 5 has no effect on protein binding of the drugs tested (digoxin, phenytoin, warfarin or indomethacin). In healthy male volunteers, the co-administration of AFADOPINE 5 does not significantly alter the effect of warfarin on prolhrombin response time.

1.3.1.6.6 PREGNANCY AND LACTATION

Safety of AFADOPINE 5 in human pregnancy or lactation has not been established.

AFADOPINE 5 does not demonstrate toxicity in animal reproductive studies other than to delay parturition and prolong labor in rats al a dose level fifty times the maximum recommended dose in humans. Accordingly, use in pregnancy is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and fetus.

1.3.1.6.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Amlodipine can have minor or moderate influence on the ability to drive and use machines. If patients taking amlodipine suffer from dizziness, headache, fatigue or nausea the ability to react may be impaired. Caution is recommended especially at the start of treatment

1.3.1.6.8 UNDESIRABLE EFFECTS

AFADOPINE 5 is well tolerated. In placebo controlled clinical trials involving patients with hypertension or angina, the most commonly observed side effects were headache, edema, fatigue, somnolence, nausea, abdominal pain, flushing, palpitation and dizziness. In these clinical trials no pattern of clinically significant laboratory test abnormalities related to AFADOPINE 5 has been observed.

Less commonly observed side effects include alopecia, altered bowel habit, arthralgia, asthenia, back pain, dyspepsia, dyspnea, gingival hyperplasia, gynecomastia, hyperglycemia, impotence, increased urinary frequency, leucopenia, malaise, mood changes, dry mouth, muscle cramps, myalgia, peripheral neuropathy, pancreatitis, increased sweating, syncope, thrombocytopenia, vasculitis, and visual disturbances and rarely, erythema multiforme. In many cases, causal association is uncertain.

Rarely, allergic reaction including pruritus, rash, angioedema and erythema multiforme hepatitis, jaundice and hepatic enzyme elevation have also been reported very infrequently (mostly consistent with cholestasis) some cases severe enough to require hospitalization have been reported in association with use of amlodipine. In many instances, causal association is uncertain.

As with other calcium channel blockers the following adverse events have been rarely reported and cannot be distinguished from the natural history of the underlying disease: myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation) and chest pain.

1.3.1.6.9 OVERDOSE

In humans, experience with intentional overdose is limited. Gastric lavage may be worthwhile in some cases. Available data suggest

that gross overdose could result in excessive peripheral vasodilatation with subsequent marked and probably prolonged systemic hypotension. Clinically significant hypotension due lo AFADOPINE 5 overdose calls for active cardiovascular support including frequent monitoring of cardiac and respiratory function, elevation of extremities and attention to circulating fluid volume and urine output. A vasoconslrictor may be helpful in restoring vascular lone and blood pressure, provided that there is no contraindication to its use. Intravenous calcium gluconate may be beneficial in reversing the effects of calcium channel blockade. Since AFADOPINE 5 is highly protein-bound, dialysis is not likely to be of benefit.

1.3.1.7 PHARMACOLOGICAL PROPERTIES

1.3.1.7.1 Pharmacodynamic properties

AFADOPINE 5 has been safely administered with thiazide diuretics, alpha blockers, beta-blockers, angiotensin-converting enzyme inhibitors, long acting nitrates, sublingual nitroglycerin, non-steroidal anti-inflammatory drugs, antibiotics and oral hypoglycemic drugs. Special studies have indicated that the co-administration of AFADOPINE 5 wilh digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers and that co-administration of cimetidine did not alter the pharmacokinetics of amlodipine.

In vitro data from human plasma studies indicate that AFADOPINE 5 has no effect on protein binding of the drugs tested (digoxin, phenytoin, warfarin or indomethacin). In healthy male volunteers, the co-administration of AFADOPINE 5 does not significantly alter the effect of warfarin on prolhrombin response time.

1.3.1.7.2 Pharmacokinetic properties

After oral administration of therapeutic dose, AFADOPINE 5 is well absorbed with peak blood levels taking place between 6-12 hours post dose. Absolute bioavailability has been estimated to be between 64 and 80 %. The volume of distribution is approximately

21 kg. Steady state plasma levels are reached after 7-8 days of consecutive dosing. Absorption of AFADOPINE 5 is unaffected by consumption of food. The terminal plasma elimination half-life is about 35-50 hours and is consistent with once daily dosing. AFADOPINE 5 is extensively metabolized by the liver to inactive metabolites with 10% of the parent compound and 60% of metabolites excreted in the urine. Hemodynamic studies and exercise based controlled clinical trials in NHYAclass Ill-IV heart failure patients have shown that AFADOPINE 5 did not lead lo clinical deterioration as measured by exercise tolerance, left ventricular ejection fraction and clinical symptomatology. A placebo controlled study (PRAISE) designed to evaluate patients in NHYAclass Ill-IV heart failure receiving digoxin, diuretics and ACE inhibitors has shown that AFADOPINE 5 did not lead to an increase in risk of

1.3.1.7.3 Preclinical safety data

Reproductive toxicology

Reproductive studies in rats and mice have shown delayed date of delivery, prolonged duration of labour and decreased pup survival at dosages approximately 50 times greater than the maximum recommended dosage for humans based on mg/kg.

Impairment of fertility

There was no effect on the fertility of rats treated with amlodipine (males for 64 days and females 14 days prior to mating) at doses up to 10 mg/kg/day (8 times* the maximum recommended human dose of 10 mg on a mg/m2 basis). In another rat study in which male rats were treated with amlodipine besilate for 30 days at a dose comparable with the human dose based on mg/kg, decreased plasma follicle-stimulating hormone and testosterone were found as well as decreases in sperm density and in the number of mature spermatids and Sertoli cells.

Carcinogenesis, mutagenesis

Rats and mice treated with amlodipine in the diet for two years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 mg/kg/day showed no evidence of carcinogenicity. The highest dose (for mice, similar to, and for rats twice* the maximum recommended clinical dose of 10mg on a mg/m2 basis) was close to the maximum tolerated dose for mice but not for rats.

Mutagenicity studies revealed no drug related effects at either the gene or chromosome levels.

*Based on patient weight of 50 kg

1.3.1.8. PHARMACEUTICAL PARTICULARS

1.3.1.8.1 List of excipients

Microcrystalline Cellulose
Lactose
Croscarmellose Sodium
Povidone
Isopropyl Alcohol
Bronopol
Magnesium Stearate
Colloidal Silicon Dioxide
Crospovidone
Talcum

1.3.1.8.2 Incompatibilities: Not applicable.

1.3.1.8.3 Shelf life: Three years.

1.3.1.8.4 Special precautions for storage: Store below 30°C. Protected from light.

1.3.1.8.5 Nature and contents of container

Available as Alu-Pvc blister pack of 10 tablets. Such 10 blister packed in a carton along with pack insert.

1.3.1.8.6 Special precautions for disposal and other Special handling

None

1.3.1.9 Marketed by:

APHANTEE PHARMACEUTICAL NIG .LTD.

Suit ff11,first floor,pacific complex no 9,

Awka Road, Onitsha,Anambra state,Nigeria.

1.3.1.10 Manufactured by:

McW Healthcare (P) LTD.

286, 287-A, 287-B, Sector-E,

Industrial Area, Sanwer Road,

Indore (M.P.) India