SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1 NAME OF THE MEDICINAL PRODUCT

Afrab Lisinopril 5mg Tablet

2 QUALITATIVEAND QUANTITATIVECOMPOSITION

Each tablet contains 5mg of Lisinopril

For a full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Tablet
A white tablet with AFRAB inscribed on one side and a marked line.

4 CLINICALPARTICULARS

4.1 Therapeutic indications

Afrab Lisinopril is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents

4.2 Posology and method of administration

Initial Therapy: In patients with uncomplicated essential hypertension not on diuretic therapy, the recommended initial dose is 10 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 20 to 40 mg per day administered in a single daily dose. The antihypertensive effect may diminish toward the end of the dosing interval regardless of the administered dose, but most commonly with a dose of 10 mg daily. This can be evaluated by measuring blood pressure just prior to dosing to determine whether satisfactory control is being maintained for 24 hours. If it is not, an increase in dose should be considered. Doses up to 80 mg have been used but do not appear to give greater effect. If blood pressure is not controlled with Lisinopril alone, a low dose of a diuretic may be added. Hydrochlorothiazide, 12.5 mg has been shown to provide an additive effect. After the addition of a diuretic, it may be possible to reduce the dose of Lisinopril.

Diuretic Treated Patients: In hypertensive patients who are currently being treated with a diuretic, symptomatic hypotension may occur occasionally following the initial dose of Lisinopril. The diuretic should be discontinued, if possible, for two to three days before beginning therapy with Lisinopril to reduce the likelihood of hypotension. The dosage of Lisinopril should be adjusted according to blood pressure response. If the patient’s blood

pressure is not controlled with Lisinopril alone diuretic therapy may be resumed as described above.

4.3 Contra-indications

Lisinopril is contraindicated in patients who are hypersensitive to this product and in patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor and in patients with hereditary or idiopathic angioedema.

4.4 Special warnings and precautions for use

Aortic Stenosis/Hypertrophic Cardiomyopathy: As with all vasodilators, lisinopril should be given with caution to patients with obstruction in the outflow tract of the left ventricle. Impaired Renal Function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin converting enzyme inhibitors, including Lisinopril, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death. In hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine may occur. Experience with another angiotensin-converting enzyme inhibitor suggests that these increases are usually reversible upon discontinuation of Lisinopril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy. Some patients with hypertension or heart failure with no apparent pre-existing renal vascular disease have developed increases in blood urea nitrogen and serum creatinine, usually minor and transient, especially when Lisinopril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or Lisinopril may be required. Patients with acute myocardial infarction in the GISSI-3 trial treated with Lisinopril had a higher (2.4% versus 1.1%) incidence of renal dysfunction in-hospital and at six weeks (increasing creatinine concentration to over 3 mg/dL or a doubling or more of the baseline serum creatinine concentration). In acute myocardial infarction, treatment with Lisinopril should be initiated with caution in patients with evidence of renal dysfunction, defined as serum creatinine concentration exceeding 2 mg/d

4.5 Interaction with other medicinal products and other forms of interaction

Hypotension - Patients on Diuretic Therapy: Patients on diuretics and especially those, in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with Lisinopril. The possibility of hypotensive effects with Lisinopril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with Lisinopril. If it is necessary to continue the diuretic, initiate therapy with Lisinopril at a dose of 5 mg daily, and provide close medical supervision after the initial dose until blood pressure has stabilized. When a diuretic is added to the therapy of a patient receiving Lisinopril, an additional antihypertensive effect is usually observed. Studies with ACE inhibitors in combination with diuretics indicate that the

dose of the ACE inhibitor can be reduced when it is given with a diuretic. Antidiabetics: Epidemiological studies have suggested that concomitant administration of ACE inhibitors and antidiabetic medicines (insulins, oral hypoglycemic agents) may cause an increased blood-glucose-lowering effect with risk of hypoglycemia. This phenomenon appeared to be more likely to occur during the first weeks of combined treatment and in patients with renal impairment. In diabetic patients treated with oral antidiabetic agents or insulin, glycemic control should be closely monitored for hypoglycemia, especially during the first month of treatment with an ACE inhibitor. Non-steroidal Anti-inflammatory Agents: In some patients with comprised renal function who are being treated with non-steroidal anti-inflammatory drugs, the co-administration of lisinopril may result in further deterioration of renal function. These effects are usually reversible. In a study in 36 patients with mild to moderate hypertension where the antihypertensive effects of Lisinopril alone were compared to Lisinopril given concomitantly with indomethacin, the use of indomethacin was associated with a reduced effect, although the difference between the two regimens was not significant. Other Agents: Lisinopril has been used concomitantly with nitrates and/or digoxin without evidence of clinically significant adverse interactions. This included post myocardial infarction patients who were receiving intravenous or transdermal nitroglycerin. No clinically important pharmacokinetic interactions occurred when Lisinopril was used concomitantly with propranolol or hydrochlorothiazide. The presence of food in the stomach does not alter the bioavailability of Lisinopril. Agents Increasing Serum Potassium: Lisinopril attenuates potassium loss caused by thiazide-type diuretics. Use of Lisinopril with potassium-sparing diuretics (e.g., spironolactone, eplerenone, triamterene or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. Potassium-sparing agents should generally not be used in patients with heart failure who are receiving Lisinopril. Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. Lithium toxicity was usually reversible upon discontinuation of lithium and the ACE inhibitor. It is recommended that serum lithium levels be monitored frequently if Lisinopril is administered concomitantly with lithium.

4.6 Pregnancy and Lactation

Pregnancy

The use of ACE inhibitors is not recommended during the first trimester of pregnancy. The use of ACE inhibitors is contraindicated during the second and third trimester of pregnancy.

ACE inhibitors should not be initiated during pregnancy. Unless continued ACE inhibitor therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy.

Lactation

Use of Lisinopril is not recommended during breast-feeding.

4.7 Effects on ability to drive and use machines

When driving vehicle or operating machines. It should be taken into account that occasionally dizziness, tiredness or confussion may occur.

4.8 Undesirable effects

- Headache
- Dizziness
- Cough
- Difficulty swallowing or breathing
- Fatigue
- Diarrhea
- Hypotension
- Kidney dysfunction

4.9 Overdose

Symptoms associated with overdosage of ACE inhibitors may include hypotension,circulatory shock,electrolyte disturbances,renal failure,hyperventilation,tachycardia.palpitations,bradycardia,dizziness,anxiety and cough.

The recommended treatment of overdose is intravenous infusion of normal saline solution. Ifhypotension occurs,the patient should be placed in the shock position. If available,treatment with angiotensin 11 infusion and /or intravenous catecholamines may also be considered.

5 PHARMACOLOGICALPROPERTIES

5.1 Pharmacodynamic Properties

Pharmcotherapeutic group: Angiotensin converting enzyme inhibitors,ATC code: C09A A03

Lisinopril inhibits ACE activity, thereby reducing plasma angiotensin II and aldosterone and increasing plasma renin activity. Lisinopril produces a smooth, gradual blood pressure (BP) reduction in hypertensive patients without affecting heart rate or cardiovascular reflexes.

Mechanism of Action

Lisinopril is a peptidyl dipeptidase inhibitor. It inhibits the angiotensin converting enzyme (ACE) that catalyses the conversion of angiotensin I to the vasoconstrictor peptide,angiotensin II. Angiotensin II also stimulate aldosterone secretion. The latter decrease may result in an increase in serum potassium concentration.

5.2 Pharmacokinetic Properties

The angiotensin-converting enzyme inhibitor, lisinopril, has an oral bioavailability of 25 percent +/- 4 percent, which is unaffected by food. The accumulation half-life averages 12.6 hours despite a terminal serum half-life of approximately 40 hours.

5.3 Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Corn starch, Aerosil, Magnesium stearate, Povidon PVP-30, Lactose powder,Pregel starch, Sodium starch glycollate and Talcum powder.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3years.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

PVC/ PVDC with Aluminium blisters contains 2 x 14 and 3 x 10 tablets packed in a printed cardboard case with a folded package insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Afrab Chem Limited
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