1. Name of Drug Product- MULTICHRIS RAMIPRIL CAPSULES 5 MG

2. Composition-

Each Capsule Contains:
Ramipril BP 5 mg
Excipients Q.S.
Approved colours used in capsules shells.

Quantitative Formula-

Sr. No	Name of Raw Material	Spec	Label claim / cap	% Overage	Qty per Capsule	Std. Qty for 2.0 Lac
1.	* Ramipril	BP	5 MG	0 %	5.00 MG	1.00 KG
2.	Maize Starch	BP			55.50 MG	11.10 KG
3.	Lactose	BP			80.00 MG	16.00 KG
4.	Colloidal silicon dioxide	BP			1.00 MG	0.20 KG
5.	Purified Talc	BP			2.00 MG	0.40 KG
6.	Magnesium Stearate	BP			1.50 MG	0.30 KG
7.	Croscarmellose sodium	BP			5.00 MG	1.00 KG
8.	Empty printed hard gelatin capsule CARAMEL/ WHITE with R-5 size "4"	IHS	1 NO'S	2 %	1.00 NO'S	204000 NO'S
	Total				**150.00 MG**	**30.00 KG**

PHARMACEUTIC

3. PHARMACEUTICAL FORM

Capsule
A White Colour Powder Filled in CARAMEL/WHITE with R-5 printed Hard Gelatin Capsule.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of hypertension.

Cardiovascular prevention: reduction of cardiovascular morbidity and mortality in patients with:
Manifest atherothrombotic cardiovascular disease (history of coronary heart disease or stroke, or peripheral vascular disease) or
Diabetes with at least one cardiovascular risk factor (see section 5.1).

- Treatment of renal disease:

- Incipient glomerular diabetic nephropathy as defined by the presence of microalbuminuria,
- Manifest glomerular diabetic nephropathy as defined by macroproteinuria in patients with at least one cardiovascular risk factor (see section 5.1),
- Manifest glomerular non diabetic nephropathy as defined by macroproteinuria ≥ 3 g/day
- Treatment of symptomatic heart failure.

- Secondary prevention after acute myocardial infarction: reduction of mortality from the acute phase of myocardial infarction in patients with clinical signs of heart failure when started > 48 hours following acute myocardial infarction.

4.2 Posology and method of administration

Ramipril is a hard gelatin capsule that comes in three strengths: 1.25 mg, 2.5 mg, **5 mg**, and 10 mg.

Posology

It is recommended that Ramipril Capsules are taken each day at the same time of the day.

Ramipril Capsules can be taken before, with or after meals, because food intake does not modify its bioavailability (see section 5.2).

Ramipril Capsules have to be swallowed with liquid. It must not be chewed or crushed.

Adults

Diuretic-Treated patients

Hypotension may occur following initiation of therapy with Ramipril Capsules; this is more likely in patients who are being treated concurrently with diuretics. Caution is therefore recommended since these patients may be volume and/or salt depleted.

If possible, the diuretic should be discontinued 2 to 3 days before beginning therapy with Ramipril Capsules (see section 4.4).

In hypertensive patients in whom the diuretic is not discontinued, therapy with Ramipril Capsules should be initiated with a 1.25 mg dose. Renal function and serum potassium should be monitored. The subsequent dosage of Ramipril Capsules should be adjusted according to blood pressure target.

Hypertension

The dose should be individualised according to the patient profile (see section 4.4) and blood pressure control.

Ramipril Capsules may be used in monotherapy or in combination with other classes of antihypertensive medicinal products (see sections 4.3, 4.4, 4.5 and 5.1).

Starting dose

Ramipril Capsules should be started gradually with an initial recommended dose of 2.5 mg daily.

Patients with a strongly activated renin-angiotensin-aldosterone system may experience an excessive drop in blood pressure following the initial dose. A starting dose of 1.25 mg is recommended in such patients and the initiation of treatment should take place under medical supervision (see section 4.4).

Titration and maintenance dose

The dose can be doubled at interval of two to four weeks to progressively achieve target blood pressure; the maximum permitted dose of ramipril is 10 mg daily. Usually the dose is administered once daily.

Cardiovascular prevention

Starting dose

The recommended initial dose is 2.5 mg of ramipril once daily.

Titration and maintenance dose

Depending on the patient's tolerability to the active substance, the dose should be gradually increased. It is recommended to double the dose after one or two weeks of treatment and - after another two to three weeks - to increase it up to the target maintenance dose of 10 mg ramipril once daily.

See also posology on diuretic treated patients above.

Treatment of renal disease

In patients with diabetes and microalbuminuria:

Starting dose:

The recommended initial dose is 1.25 mg of ramipril once daily.

Titration and maintenance dose

Depending on the patient's tolerability to the active substance, the dose is subsequently increased. Doubling the once daily dose to 2.5 mg after two weeks and then to 5 mg after a further two weeks is recommended.

In patients with diabetes and at least one cardiovascular risk

Starting dose:

The recommended initial dose is 2.5 mg of ramipril once daily.

Titration and maintenance dose

Depending on the patient's tolerability to the active substance, the dose is subsequently increased. Doubling the daily dose to 5 mg ramipril after one or two weeks and then to 10 mg ramipril after a further two or three weeks is recommended. The target daily dose is 10 mg.

In patients with non- diabetic nephropathy as defined by macroproteinuria ≥ 3 g/day.

Starting dose:

The recommended initial dose is 1.25 mg of ramipril once daily.

Titration and maintenance dose

Depending on the patient's tolerability to the active substance, the dose is subsequently increased. Doubling the once daily dose to 2.5 mg after two weeks and then to 5 mg after a further two weeks is recommended.

Symptomatic heart failure

Starting dose

In patients stabilized on diuretic therapy, the recommended initial dose is 1.25 mg daily.

Titration and maintenance dose

Ramipril should be titrated by doubling the dose every one to two weeks up to a maximum daily dose of 10 mg. Two administrations per day are preferable.

Secondary prevention after acute myocardial infarction and with heart failure

Starting dose

After 48 hours, following myocardial infarction in a clinically and haemodynamically stable patient, the starting dose is 2.5 mg twice daily for three days. If the initial 2.5 mg dose is not tolerated a dose of 1.25 mg twice a day should be given for two days before increasing to 2.5 mg and 5 mg twice a day. If the dose cannot be increased to 2.5 mg twice a day the treatment should be withdrawn.

See also posology on diuretic treated patients above.

Titration and maintenance dose

The daily dose is subsequently increased by doubling the dose at intervals of one to three days up to the target maintenance dose of 5 mg twice daily.

The maintenance dose is divided in 2 administrations per day where possible.

If the dose cannot be increased to 2.5 mg twice a day treatment should be withdrawn.

Sufficient experience is still lacking in the treatment of patients with severe (NYHA IV) heart failure immediately after myocardial infarction. Should the decision be taken to treat these patients, it is recommended that therapy be started at 1.25 mg once daily and that particular caution be exercised in any dose increase.

Special populations

Patients with renal impairment

Daily dose in patients with renal impairment should be based on creatinine clearance (see section 5.2):

- if creatinine clearance is ≥ 60 ml/min, it is not necessary to adjust the initial dose (2.5 mg/day); the maximal daily dose is 10 mg;

- if creatinine clearance is between 30-60 ml/min, it is not necessary to adjust the initial dose (2.5 mg/day); the maximal daily dose is 5 mg;

- if creatinine clearance is between 10-30 ml/min, the initial dose is 1.25 mg/day and the maximal daily dose is 5 mg;

- in haemodialysed hypertensive patients: ramipril is slightly dialysable; the initial dose is 1.25 mg/day and the maximal daily dose is 5 mg; the medicinal product should be administered few hours after haemodialysis is performed.

Patients with hepatic impairment

In patients with hepatic impairment, treatment with Ramipril Capsules must be initiated only under close medical supervision and the maximum daily dose is 2.5 mg ramipril.

Elderly

Initial doses should be lower and subsequent dose titration should be more gradual because of greater chance of undesirable effects especially in very old and frail patients. A reduced initial dose of 1.25 mg ramipril should be considered.

Paediatric population

The safety and efficacy of ramipril in children has not yet been established. Currently available data for ramipril are described in sections 4.8, 5.1, 5.2 & 5.3 but no specific recommendation on posology can be made.

Method of administration: Oral use. The capsules should be taken whole.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients or any other ACE (Angiotensin Converting Enzyme) inhibitors.

- History of angioedema (hereditary, idiopathic or due to previous angioedema with ACE inhibitors or AIIRAs)

- Extracorporeal treatments leading to contact of blood with negatively charged surfaces - Significant bilateral renal artery stenosis or renal artery stenosis in a single functioning kidney

- 2nd and 3rd trimester of pregnancy

- Ramipril must not be used in patients with hypotensive or haemodynamically unstable states.

- The concomitant use of Ramipril with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m^2).

4.4 Special warnings and precautions for use

Anaphylactoid and Possibly Related Reactions
Presumably because drugs that act directly on the renin-angiotensin-aldosterone system (e.g., ACE inhibitors) affect the metabolism of eicosanoids and polypeptides, including endogenous bradykinin, patients receiving these drugs (including Ramipril) may be subject to a variety of adverse reactions, some of them serious.

Angioedema
Head and Neck Angioedema
Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor.
Angioedema of the face, extremities, lips, tongue, glottis, and larynx has been reported in patients treated with ACE inhibitors. Angioedema associated with laryngeal edema can be fatal. If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, discontinue treatment with Ramipril and institute appropriate therapy immediately. Where there is involvement of the tongue, glottis, or larynx likely to cause airway obstruction, administer appropriate therapy (e.g., subcutaneous epinephrine solution 1:1000 [0.3 mL to 0.5 mL]).
In considering the use of Ramipril, note that in controlled clinical trials ACE inhibitors cause a higher rate of angioedema in Black patients than in non-Black patients.
In a large U.S. post-marketing study, angioedema (defined as reports of angio, face, larynx, tongue, or throat edema) was reported in 3/1523 (0.20%) Black patients and in 8/8680 (0.09%) non-Black patients. These rates were not different statistically.

Patients taking concomitant mammalian target of rapamycin (mTOR) inhibitor (e.g. temsirolimus) therapy or a neprilysin inhibitor may be at increased risk for angioedema.

Intestinal Angioedema
Intestinal angioedema has been reported in patients treated with ACE inhibitors. These patients presented with abdominal pain (with or without nausea or vomiting); in some cases there was no prior history of facial angioedema and C-1 esterase levels were normal. The angioedema was diagnosed by procedures including abdominal CT scan or ultrasound, or at surgery, and symptoms resolved after stopping the ACE inhibitor. Include intestinal angioedema in the differential diagnosis of patients on ACE inhibitors presenting with abdominal pain.

Anaphylactoid Reactions during Desensitization
Two patients undergoing desensitizing treatment with hymenoptera venom while receiving ACE inhibitors sustained life-threatening anaphylactoid reactions. In the same patients, these reactions were avoided when ACE inhibitors were temporarily withheld, but they reappeared upon inadvertent rechallenge.

Anaphylactoid Reactions during Membrane Exposure
Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes and treated concomitantly with an ACE inhibitor. Anaphylactoid reactions have also been reported in patients undergoing low-density lipoprotein apheresis with dextran sulfate absorption.

Hepatic Failure and Impaired Liver Function
Rarely, ACE inhibitors, including Ramipril, have been associated with a syndrome that starts with cholestasis jaundice and progresses to fulminant hepatic necrosis and sometimes death. The mechanism of this syndrome is not understood. Discontinue Ramipril if patient develops jaundice or marked elevations of hepatic enzymes.
As Ramipril is primarily metabolized by hepatic esterases to its active moiety, Ramiprilat, patients with impaired liver function could develop markedly elevated plasma levels of Ramipril. No formal pharmacokinetic studies have been carried out in hypertensive patients with impaired liver function.

Renal Impairment
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 ACE inhibitors, including Ramipril, may be associated with oliguria or progressive azotaemia and rarely with acute renal failure 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 ACE inhibitor suggests that these increases would be reversible upon discontinuation of Ramipril and/or diuretic therapy. In such patients, monitor renal function during the first few weeks of therapy. Some hypertensive patients with no apparent pre-existing renal vascular disease have developed increases in blood urea nitrogen and serum creatinine, usually minor and transient, especially when Ramipril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction of Ramipril and/or discontinuation of the diuretic may be required.

Neutropenia and Agranulocytosis
In rare instances, treatment with ACE inhibitors may be associated with mild reductions in red blood cell count and haemoglobin content, blood cell or platelet counts. In isolated cases, agranulocytosis, pancytopenia, and bone marrow depression may occur. Hematological reactions to ACE inhibitors are more likely to occur in patients with collagen-vascular disease (e.g., systemic lupus erythematosus, scleroderma) and renal impairment. Consider monitoring white blood cell counts in patients with collagen-vascular disease, especially if the disease is associated with impaired renal function.

Hypotension General Considerations
Ramipril can cause symptomatic hypotension, after either the initial dose or a later dose when the dosage has been increased. Like other ACE inhibitors, Ramipril, has been only rarely associated with hypotension in uncomplicated hypertensive patients. Symptomatic hypotension is most likely to occur in patients who have been volume-and/or salt-depleted as a result of prolonged diuretic therapy, dietary salt restriction, dialysis, diarrhea, or vomiting. Correct volume-and salt-depletion before initiating therapy with Ramipril.
If excessive hypotension occurs, place the patient in a supine position and, if necessary, treat with intravenous infusion of physiological saline. Ramipril treatment usually can be continued following restoration of blood pressure and volume.

Heart Failure Post-Myocardial Infarction
In patients with heart failure post-myocardial infarction who are currently being treated with a diuretic, symptomatic hypotension occasionally can occur following the initial dose of Ramipril. If the initial dose of 2.5 mg Ramipril cannot be tolerated, use an initial dose of 1.25 mg Ramipril to avoid excessive hypotension. Consider reducing the dose of concomitant diuretic to decrease the incidence of hypotension.

Congestive Heart Failure
In patients with congestive heart failure, with or without associated renal insufficiency, ACE inhibitor therapy may cause excessive hypotension, which may be associated with oliguria or azotemia and rarely, with acute renal failure and death. In such patients, initiate Ramipril therapy under close medical supervision and follow patients closely for the first 2 weeks of treatment and whenever the dose of Ramipril or diuretic is increased.

Surgery and anesthesia
In patients undergoing surgery or during anesthesia with agents that produce hypotension, Ramipril may block angiotensin II formation that would otherwise occur secondary to compensatory renin release. Hypotension that occurs as a result of this mechanism can be corrected by volume expansion.

Fetal Toxicity Pregnancy Category D
Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue Ramipril as soon as possible.

Dual Blockade of the Renin-Angiotensin System
Dual blockade of the RAS with angiotensin receptor blockers, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy. Most patients receiving the combination of two RAS inhibitors do not obtain any additional benefit compared to monotherapy. In general, avoid combined use of RAS inhibitors. Closely monitor blood pressure, renal function and electrolytes in patients on Ramipril and other agents that affect the RAS.

Hyperkalemia
In clinical trials with Ramipril, hyperkalemia (serum potassium >5.7 mEq/L) occurred in approximately 1% of hypertensive patients receiving Ramipril. In most cases, these were isolated values, which resolved despite continued therapy. None of these patients were discontinued from the trials because of hyperkalemia. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of other drugs that raise serum potassium levels. Monitor serum potassium in such patients.

Cough
Presumably caused by inhibition of the degradation of endogenous bradykinin, persistent non- productive cough has been reported with all ACE inhibitors, always resolving after discontinuation of therapy. Consider the possibility of angiotensin converting enzyme inhibitor induced-cough in the differential diagnosis of cough.

4.5 Interaction with other medicinal products and other forms of interaction
You should always tell your doctor about any prescription, non-prescription, illegal, and recreational drugs; herbal remedies; and nutritional and dietary supplements you're taking, especially:

- Aliskiren (Tekturna)
- Losartan (Cozaar), valsartan (Diovan), telmisartan (Micardis), and other ARBs
- Spironolactone (Aldactone), amiloride (Midamor), and certain other diuretics.
- Potassium supplements
- Lithium
- Gold sodium thiomalate (Myochrysine)
- Non-steroidal anti-Inflammatory drugs (NSAIDs) if you are elderly, dehydrated, or have compromised kidney function.
- Temsirolimus (Torisel), and other mTOR inhibitors used to treat kidney cancer.

4.6 Pregnancy and lactation
Ramipril can harm a developing fetus, particularly when taken during the second and third trimesters. Drugs like ramipril can reduce the kidney function of the unborn baby, as well as cause poor development of the baby's lungs and bones.

Ramipril is also associated with numerous other problems for newborns, including death. Ramipril should not be taken if you are pregnant or plan on becoming pregnant.

Ramipril is excreted in human breast milk and should not be taken if you are breastfeeding.

4.7 Effects on ability to drive and use machines
Ramipril can cause blurred vision and make some people feel dizzy, especially when they first start taking it or after taking a bigger dose. If this happens to you, do not drive a car, ride a bike, or use tools or machinery.
If you've had a stroke or a heart attack then it may not be safe for you to drive.
Talk to your doctor or pharmacist if you're unsure whether it's safe for you to drive while taking ramipril.

4.8 Undesirable effects Side

Effects

The most common side effects of ramipril are:

- Headache
- Dizziness
- Fatigue
- Cough

Less common side effects of the drug include:

- Hypotension and dizziness that occurs after standing up from a sitting or lying position
- Chest pain
- Fainting
- Vertigo
- Diarrhoea
- Vomiting
- Urinating less often and other indications of abnormal kidney function

Rare Side Effects of Ramipril

Ramipril may cause a wide range of rare health problems that may require medical attention. These include but are not limited to:

- Heart palpitations
- Jaundice (yellowing of your skin or eyes)
- Gastrointestinal issues, including abdominal pain, poor appetite (anorexia), constipation, and dry mouth.
- Light sensitivity
- Stevens-Johnson syndrome (an immune condition that causes swelling and several skin problems)
- Purple skin rash (purpura)
- Anxiety and depression
- Convulsions
- Drowsiness
- Ringing in the ears (tinnitus) and hearing loss
- Increased sweating
- Weight gain
- Laboured breathing
- Fever

4.9 Overdose

Symptoms associated with overdosage of ACE inhibitors may include excessive peripheral vasodilatation (with marked hypotension, shock), bradycardia, electrolyte disturbances, and renal failure. The patient should be closely monitored and the treatment should be symptomatic and supportive. Suggested measures include primary detoxification (gastric lavage, administration of adsorbents) and measures to restore haemodynamic stability, including, administration of alpha 1 adrenergic agonists or angiotensin II (angiotensinamide) administration. Ramiprilat, the active metabolite of ramipril is poorly removed from the general circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Single doses of Ramipril of 2.5 mg to 20 mg produce approximately 60% to 80% inhibition of ACE activity 4 hours after dosing with approximately 40% to 60% inhibition after 24 hours. Multiple oral doses of Ramipril of 2.0 mg or more cause plasma ACE activity to fall by more than 90% 4 hours after dosing, with over 80% inhibition of ACE activity remaining 24 hours after dosing. The more prolonged effect of even small multiple doses presumably reflects saturation of ACE binding sites by Ramiprilat and relatively slow release from those sites.

5.2 Pharmacokinetic properties

Absorption

Following oral administration of Ramipril, peak plasma concentrations (C max) of Ramipril are reached within 1 hour. The extent of absorption is at least 50% to 60%, and is not significantly influenced by the presence of food in the gastrointestinal tract, although the rate of absorption is reduced. In a trial in which subjects received Ramipril capsules or the contents of identical capsules dissolved in water, dissolved in apple juice, or suspended in applesauce, serum Ramiprilat levels were essentially unrelated to the use or non-use of the concomitant liquid or food.

Distribution

Cleavage of the ester group (primarily in the liver) converts Ramipril to its active diacid metabolite, Ramiprilat. Peak plasma concentrations of Ramiprilat are reached 2 to 4 hours after drug intake. The serum protein binding of Ramipril is about 73% and that of Ramiprilat about 56%; in vitro, these percentages are independent of concentration over the range of 0.01 µg/mL to 10 µg/mL.

Metabolism

Ramipril is almost completely metabolized to Ramiprilat, which has about 6 times the ACE inhibitory activity of Ramipril, and to the diketopiperazine ester, the diketopiperazine acid, and the glucuronides of Ramipril and Ramiprilat, all of which are inactive.
Plasma concentrations of Ramipril and Ramiprilat increase with increased dose, but are not strictly dose-proportional. The 24-hour AUC for Ramiprilat, however, is dose-proportional over the 2.5 mg to 20 mg dose range. The absolute bioavailabilities of Ramipril and Ramiprilat were 28% and 44%, respectively, when 5 mg of oral Ramipril was compared with the same dose of Ramipril given intravenously.
After once-daily dosing, steady-state plasma concentrations of Ramiprilat are reached by the fourth dose. Steady-state concentrations of Ramiprilat are somewhat higher than those seen after the first dose of Ramipril capsules, especially at low doses (2.5 mg), but the difference is clinically insignificant.

Plasma concentrations of Ramiprilat decline in a triphasic manner (initial rapid decline, apparent elimination phase, terminal elimination phase). The initial rapid decline, which represents distribution of the drug into a large peripheral compartment and subsequent binding to both plasma and tissue ACE, has a half-life of 2 to 4 hours. Because of its potent binding to ACE and slow dissociation from the enzyme, Ramiprilat shows two elimination phases. The apparent elimination phase corresponds to the clearance of free Ramiprilat and has a half-life of 9 to18 hours. The terminal elimination phase has a prolonged half-life (>50 hours) and probably represents the binding/dissociation kinetics of the Ramiprilat/ACE complex. It does not contribute to the accumulation of the drug. After multiple daily doses of Ramipril capsules 5 mg to 10 mg, the half- life of Ramiprilat concentrations within the therapeutic range was 13 to 17 hours.
In patients with creatinine clearance <40 mL/min/1.73 m 2, peak levels of Ramiprilat are approximately doubled, and trough levels may be as much as quintupled. In multiple-dose regimens, the total exposure to Ramiprilat (AUC) in these patients is 3 to 4 times as large as it is in patients with normal renal function who receive similar doses.
In patients with impaired liver function, the metabolism of Ramipril to Ramiprilat appears to be slowed, possibly because of diminished activity of hepatic esterases, and plasma Ramipril levels in these patients are increased about 3-fold. Peak concentrations of Ramiprilat in these patients, however, are not different from those seen in subjects with normal hepatic function, and the effect of a given dose on plasma ACE activity does not vary with hepatic function.

Excretion

After oral administration of Ramipril, about 60% of the parent drug and its metabolites are eliminated in the urine, and about 40% is found in the feces. Drug recovered in the feces may represent both biliary excretion of metabolites and/or unabsorbed drug, however the proportion of a dose eliminated by the bile has not been determined. Less than 2% of the administered dose is recovered in urine as unchanged Ramipril. The urinary excretion of Ramipril, Ramiprilat, and their metabolites is reduced in patients with impaired renal function. Compared to normal subjects, patients with creatinine clearance <40 mL/min/1.73 m 2 had higher peak and trough Ramiprilat levels and slightly longer times to peak concentrations.

5.3 Preclinical safety data

Reproduction toxicology studies in the rat, rabbit and monkey did not disclose any teratogenic properties. Fertility was not impaired either in male or in female rats. The administration of Ramipril to female rats during the fetal period and lactation produced irreversible renal damage (dilatation of the renal pelvis) in the offspring at daily doses of 50 mg/kg body weight and higher.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Maize Starch
Lactose
Colloidal silicon dioxide
Purified Talc
Magnesium Stearate
Croscarmellose sodium
Empty printed hard gelatin capsule CARAMEL/WHITE with R-5 size “4”

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Store at temperature below 30°C in a dry place. Protect from light.

6.5 Nature and Contents of Container

Pack the 2 blisters of 14 capsules in one mono carton with insert. i.e., 2 x 14 capsules.

6.6 Special Precautions for Disposal of a used medicinal product or waste materials derived from such medicinal product and Other Handling of the Product

No special requirements

7. APPLICANT/HOLDER OF CERTIFICATE OG PRODUCT REGISTRATION

MULTICHRIS PHARM & CHEMICAL COMPANY LTD.
13 Qudus Folawoyi Ehi Crescent, Off Ashirigbon Street Isolo, Lagos, Nigeria.

8. DRUG PRODUCT MANUFACTURER

RELAX BIOTECH PVT. LTD.
862/1, G.I.D.C., Makarpura, Vadodara - 390010, INDIA.

9. NAFDAC REGISTRATION NUMBER(S)

B4-8677