BRANDNAME:	**RINOSIL10**
GENERICNAME:	**LISINOPRILTABLETSBP10 MG**

PRODUCTINFORMATION

SummaryofProductCharacteristics(SmPC)Enclose

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BRANDNAME:	**RINOSIL10**
GENERICNAME:	**LISINOPRILTABLETSBP10 MG**

1. NAMEOFTHEMEDICINALPRODUCT

Rinosil10

(LisinopriltabletsBP10mg)

(Trade)nameofproductRinos

il10

Strength

LisinoprilBP10mg

PharmaceuticalForm

UncoatedTablets

2. QUALITATIVEANDQUANTITATIVECOMPOSITION

QualitativeDeclarationCo

mposition:

EachUncoatedTabletsContainsTabletscontains:

Lisinopril Dihydrate BP

EquivalencetoLisinopril..... 10mg

Excipients..... q.s.

Colour:ApprovedColour

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Sr. No.	Ingredients	Specification	UnitFormula (mg)	BatchFormula (Kg)
ACTIVEMATERIAL				
1.	LisinoprilDihydrateBP EquivalenttoLisinopril	BP	10.88	8.704*
DRYMIXING				
2.	MaizeStarch	BP	44.520	39.177**
3.	DiBasicCalciumPhosphate Dihydrates	BP	20.040	16.032
4.	PregelatinisedStarch	BP	22.500	18.000
5.	Mannitol	BP	30.00	24.000
6.	CroscarmelloseSodium	BP	7.500	6.000
BINDER				
7.	PolyVinylPyrrolidoneK-30 (PVPK-30)	BP	3.750	3.000
8.	ColourSunsetYellowSupra	IH	0.010	0.008
9.	PurifiedWater	IH	q.s.	6.400
10.	Isopropylalcohol	BP	q.s.	25.600
LUBRICANT				
11.	CroscarmelloseSodium	BP	9.000	7.200
12.	MagnesiumStearate	BP	1.800	1.440
		TotalWeightofTablet	**150.00mg**	**120.00kg**

Remarks:

*QuantityofLisinoprilDihydrateistakenaftercalculationbasedonassayand LOD.

**MaizeStarchquantitychangesaccordingtochangeinquantityofLisinoprilDihydrate.

3. PHARMACEUTICALFORM

Uncoatedtablets

4. Clinicalparticulars

4.1 **TherapeuticindicationsHy**

pertension

Treatmentofhypertension.

HeartFailure

Treatmentofsymptomaticheartfailure.

AcuteMyocardialInfarction

Short-term (6 weeks) treatment of haemodynamically stable patients within 24 hours of an acute myocardial infarction.

RenalComplicationsofDiabetesMellitus

Treatment of renal disease in hypertensive patients with Type 2 diabetes mellitus and incipient Nephropathy.Lisinoprilcanbeusedaloneorincombinationwithotherantihypertensiveagents

4.2 **PosologyandmethodofadministrationPosol ogy**

Lisinopriltabletsshouldbeadministeredorallyinasingledailydose.Aswithallothermedication Takenoncedaily,Lisinopriltabletsshouldbetakenatapproximatelythesametimeeachday.The Absorption of Lisinopril tablets is not affected by food.

Thedoseshouldbeindividualizedaccordingtopatientprofileandbloodpressureresponse

Hypertension

Lisinopriltabletsmaybeusedasmonotherapyorincombinationwithotherclassesof antihypertensive therapy.

Startingdose

In patients with hypertension the usual recommended starting dose is 10 mg. Patients with a stronglyactivatedrenin-angiotensin-aldosteronesystem(inparticular,renovascularhypertension, salt and /or volume depletion, cardiac decompensation, or severe hypertension) may experience an excessive blood pressure fall following the initial dose. A starting dose of 2.5-5 mg is recommended in such patients and the initiation of treatment should take place under medical supervision. A lower starting dose is required in the presence of renal impairment.

Maintenancedose

Theusualeffectivemaintenancedosageis20mgadministeredinasingledailydose.Ingeneralif thedesiredtherapeuticeffectcannotbeachievedinaperiodof2to4weeksonacertaindoselevel, thedosecanbe furtherincreased.Themaximum doseusedinlong-term,controlledclinical trials was 80 mg/day.

Diuretic-TreatedPatients

Symptomatic hypotension mayoccur following initiation of therapy with Lisinopril tablets. This is morelikelyin patients who arebeingtreated currentlywith diuretics. Caution is recommended therefore,sincethesepatientsmaybevolumeand/orsaltdepleted. Ifpossible,thediureticshould bediscontinued2to3daysbeforebeginningtherapywithLisinopriltablets.Inhypertensive patients in whom the diuretic cannot be discontinued, therapy with Lisinopril tablets should beinitiatedwitha5mgdose.Renalfunctionandserumpotassiumshouldbemonitored.The subsequent dosage of Lisinopril tablets should be adjusted according to blood pressure response. If required, diuretic therapy may be resumed

4.3 Contraindications

Hypersensitivity to Lisinopril tablets, to any of the excipients listed in or any other angiotensin converting enzyme (ACE) inhibitor.

- HistoryofangioedemaassociatedwithpreviousACEinhibitortherapy
- Hereditaryoridiopathicangioedema
- Secondandthirdtrimestersofpregnancy.
- In combination with aliskiren-containing medicines in patients with diabetes mellitus (type I or II) Or with moderate to severe renal impairment (GFR < 60 ml/min/1.73m^2

4.4 Specialwarningsandprecautionsforuse

Symptomatic hypotension is seen rarely in uncomplicated hypertensive patients. In hypertensive patients receiving Lisinopril tablets, hypotension is more likely to occur if the patient has been volume-depleted e.g. by diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting, or has severe renin-dependent hypertension. In patients with heart failure, with or without associatedrenalinsufficiency,symptomatichypotensionhasbeenobserved.Thisismostlikelyto occur in those patients with more severe degrees of heart failure, as reflected by the use of high dosesofloopdiuretics,hyponatremiaorfunctionalrenalimpairment.Inpatientsatincreasedrisk of symptomatic hypotension, initiation of therapy and dose adjustment should be closely monitored.Similarconsiderationsapplytopatientswithischemicheartorcerebrovasculardisease inwhomanexcessivefallinbloodpressurecouldresultinamyocardialinfarctionor

cerebrovascularaccident.Ifhypotensionoccurs,thepatientshouldbeplacedinthesupineposition and,ifnecessary,shouldreceiveanintravenousinfusionofnormalsaline.Atransienthypotensive response is not a contraindication to further doses, which can be given usually without difficulty oncethebloodPressure hasincreasedaftervolumeexpansion.Insomepatientswithheartfailure whohavenormalorlowbloodpressure,additionalloweringofsystemicbloodpressuremayoccur with Lisinopril tablets. This effect is anticipated and is not usually a reason to discontinue treatment. If hypotension becomes symptomatic, a reduction of dose or discontinuation of Lisinopril tablets maybe necessary. Hypotension in Acute Myocardial Infarction Treatment with Lisinopril tablets must not be initiated in acute myocardial infarction patients who are at risk of further serious haemodynamic deterioration after treatment with a vasodilator. These are patients withsystolicbloodpressureof100mmHgorlowerorthoseincardiogenicshock.Duringthefirst 3 days following the infarction, the dose should be reduced if the systolic blood pressure is 120 mmHgorlower.Maintenancedosesshouldbereducedto5mgortemporarilyto2.5mgifsystolic blood pressure is 100 mm Hg or lower. If hypotension persists (systolic blood pressure less than 90 mm Hg for more than 1 hour) then Lisinopril tablets should be withdrawn. Aortic and mitral valve stenosis / hypertrophic cardiomyopathy as with other ACE inhibitors, Lisinopril tablets should be given with caution to patients with mitral valve stenosis and obstruction in the outflow of the left ventricle such as aortic stenosis or hypertrophic cardiomyopathy.

RenalFunctionImpairment

Incasesofrenalimpairment(creatinineclearance<80ml/min),theinitialLisinopriltabletsdosage should be adjusted according to the patient's creatinine clearance and then as a function of the patient's response to treatment. Routine monitoring of potassium and creatinine is part of normal medical practice for these patients.

AnaphylactoidreactionsinHaemodialysisPatients

Anaphylactoid reactions have been reported in patients dialyzed with high flux membranes (e.g. AN 69) and treated concomitantly with an ACE inhibitor. In these patients consideration should begiventousingadifferenttypeofdialysismembraneordifferentclassofantihypertensiveagent.

Anaphylactoidreactionsduringlow-densitylipoproteins(LDL)apheresis

Rarely, patients receiving ACE inhibitors during low-density lipoproteins (LDL) apheresis with dextransulphatehave experiencedlife-threateninganaphylactoidreactions.These reactionswere avoided by temporarily withholding ACE inhibitor therapy prior to each apheresis.

Desensitization

PatientsreceivingACEinhibitorsduringdesensitizationtreatment(e.g.hymenopteravenom)have sustained anaphylactoid reactions. In the same patients, these reactions have been avoided when ACE inhibitors were temporarily withheld but they have reappeared upon inadvertent readministration of the medicinal product.

4.5 **InteractionwithothermedicinalproductsandotherformsofinteractionAntihyp ertensiveagents**

WhenLisinopriltabletsiscombinedwithotherantihypertensiveagents(e.g.glyceryltrinitrateand othernitrates,orothervasodilators),additivefallsinbloodpressuremayoccur.Clinicaltrialdata has shown that dual blockade of the renin-angiotensin-aldosterone system (RAAS) through the combineduseofACE-inhibitors,angiotensinIIreceptorblockersoraliskirenisassociatedwitha higher frequency of adverse events such as hypotension, hyperkalemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS acting agent .

Drugsthatmayincreasetheriskofangioedema

ConcomitanttreatmentofACEinhibitorswithmammaliantargetofrapamycin(mTOR)inhibitors (e.g. temsirolimus, sirolimus, everolimus) or neutral endopeptidase (NEP) inhibitors (e.g. racecadotril) or tissue plasminogen activator may increase the risk of angioedema.

Diuretics

Whenadiureticisaddedtothetherapyofapatientreceiving Lisinopriltabletstheantihypertensive effect is usually additive. Patients already on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure when Lisinopril tablets is added. The possibility of symptomatic hypotension with Lisinopril tablets can be minimized by discontinuing the diuretic prior to initiation of treatment with Lisinopril tablets. Potassium supplements, potassium-sparing diuretics or potassium- containing salt substitutes and other drugs that may increase serum potassium levels although in

clinicaltrials,serumpotassiumusuallyremained withinnormallimits,hyperkalemiadidoccurin some patients. The use of potassium supplements, potassium-sparing diuretics or potassium-containing salt substitutes and other drugs that may increase serum potassium levels, particularly in patients with impaired renal function, may lead to a significant increase in serum potassium.

4.6 **Fertility,pregnancyandlactation**

Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitorsduringthefirsttrimesterofpregnancyhasnotbeenconclusive;howeverasmallincrease in risk cannot be excluded. 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. When pregnancy is diagnosed, treatment withACEinhibitorsshouldbestoppedimmediately,and,ifappropriate,alternativetherapyshould be started. Exposure to ACE inhibitor therapyduring the second and third trimesters is known to induce human foetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation)andneonataltoxicity(renalfailure,hypotension,hyperkalaemia).Shouldexposureto ACE inhibitor have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended. Infants whose mothers have taken ACE inhibitors should be closely observed for hypotension.

Breast-feeding

Because no information is available regarding the use of Lisinopril tablet during breastfeeding, Lisinopril tablet is not recommended and alternative treatments with better established safety Profilesduringbreast-feedingarepreferable,especiallywhilenursinganewbornorpreterminfant.

4.7 **Effectsonabilitytodriveandusemachines**

Whendrivingvehiclesoroperatingmachinesitshouldbetakenintoaccountthatoccasionally Dizziness or tiredness may occur.

4.8 **Undesirableeffects**

Thefollowingundesirableeffectshavebeenobservedandreportedduringtreatmentwith

LisinopriltabletsandotherACEinhibitorswiththefollowingfrequencies:Verycommon(≥1/10), Common(≥1/100to<1/10),uncommon(≥1/1,000to<1/100),rare(≥1/10,000to<1/1,000),very Rare (<1/10,000), not known

Bloodandthelymphaticsystemdisorders:

Rare:decreasesinhaemoglobin,decreasesinhaematocrit.

Veryrare:bonemarrowdepression,anaemia,thrombocytopenia,leucopenia,neutropenia, Agranulocytosis, haemolytic anaemia, lymphadenopathy, autoimmune disease

Immunesystemdisorders

Notknown:anaphylactic/anaphylactoidreaction

Endocrine Disorders

Rare:syndromeofinappropriateantidiuretichormonesecretion(SIADH)

Metabolismandnutritiondisorders

Veryrare:hypoglycemia

Nervoussystemandpsychiatricdisorders:

Common:dizziness,headache

Uncommon:moodalterations,paraesthesia,vertigo,tastedisturbance,sleepdisturbances, hallucinations.

Rare:mentalconfusion,olfactorydisturbance Not

known: depressive symptoms, syncope.

Cardiacandvasculardisorders:

Common:orthostaticeffects(includinghypotension)

Uncommon:myocardialinfarctionorcerebrovascularaccident,possiblysecondarytoexcessive

Hypotension in high risk patients, palpitations, tachycardia. Raynaud's phenomenon

Respiratory,thoracicandmediastinaldisorders:

Common: cough

Uncommon:rhinitis

Veryrare:bronchospasm,sinusitis,allergicalveolitis/eosinophilicpneumonia

Gastrointestinaldisorders:

Common:diarrhoea,vomiting

Uncommon:nausea,abdominalpainandindigestion Rare:
dry mouth
Veryrare:pancreatitis,intestinalangioedema,hepatitis-eitherhepatocellularorcholestatic, jaundice and hepatic failure

Skinandsubcutaneoustissuedisorders:

Uncommon:rash,pruritus
Rare:hypersensitivity/angioneuroticoedema:angioneuroticoedemaoftheface,extremities,lips, Tongue, glottis, and/or larynx, urticaria, alopecia, psoriasis
Veryrare:sweating,pemphigus,toxicepidermalnecrolysis,Stevens-Johnsonsyndrome,erythema multiforme, cutaneous pseudo lymphoma

4.9 **Overdose**

Limiteddataareavailableforoverdoseinhumans.SymptomsassociatedwithoverdosageofACE 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. If hypotensionoccurs,thepatientshouldbeplacedintheshockposition.Ifavailable,treatmentwith angiotensin IIinfusion and/or intravenous catecholamines mayalso be considered. If ingestion is recent, take measures aimed at eliminating Lisinopril tablets (e.g., emesis, gastric lavage, administration of absorbents and sodium sulphate). Lisinopril tablets may be removed from the general circulation by haemodialysis. Pacemaker therapy is indicated for therapy-resistant bradycardia. Vital signs, serum electrolytes and creatinine concentrations should be monitored frequently.

5. Pharmacologicalproperties

5.1 **Pharmacodynamicproperties**

Pharmacotherapeuticgroup: Angiotensinconvertingenzymeinhibitors**,ATCcode:**C09AA03

Mechanismofaction

Lisinopriltabletsisapeptidyldipeptidaseinhibitor.Itinhibitstheangiotensinconvertingenzyme (ACE)thatcatalysestheconversionofangiotensinItothevasoconstrictorpeptide,angiotensinII.

Angiotensin II also stimulates aldosterone secretion by the adrenal cortex. Inhibition of ACE results in decreased concentrations of angiotensin II which results in decreased vasopressor activityand reduced aldosterone secretion. The latter decrease mayresult in an increase in serum potassium concentration.

Pharmacodynamiceffects

WhilstthemechanismthroughwhichLisinoprillowersbloodpressureisbelievedtobeprimarily

Suppression of the renin-angiotensin-aldosterone system, Lisinopril is antihypertensive even in Patients with low renin hypertension. ACE is identical to kinase II, an enzyme that degrades bradykinin. Whether increased levels of bradykinin, a potent vasodilatory peptide, play a role in the therapeutic effects of Lisinopril remains to be elucidated.

5.2 **PharmacokineticpropertiesAbs**

orption

FollowingoraladministrationofLisinopril,peakserumconcentrationsoccurwithinabout7hours, although there was a trend to a small delay in time taken to reach peak serum concentrations in acutemyocardial infarctionpatients.Basedonurinaryrecovery,themean extent ofabsorptionof Lisinoprilisapproximately25%withinter-patientvariabilityof6-60%overthedoserangestudied (5-80 mg). The absolute bioavailability is reduced approximately 16% in patients with heart failure. Lisinopril absorption is not affected by the presence of food.

Distribution

Lisinopril does not appear to be bound to serum proteins other than to circulating angiotensin converting enzyme (ACE). Studies in rats indicate that Lisinopril crosses the blood-brain barrier poorly.

Elimination

Lisinopril does not undergo metabolism and is excreted entirely unchanged into the urine. On multiple dosingLisinopril has an effective half-life of accumulation of 12.6 hours. The clearance of Lisinopril in healthy subjects is approximately 50 ml/min. Declining serum concentrations exhibitaprolongedterminalphase,whichdoesnotcontributetodrugaccumulation.Thisterminal phase probably represents saturable binding to ACE and is not proportional to dose.

Hepaticimpairment

ImpairmentofhepaticfunctionincirrhoticpatientsresultedinadecreaseinLisinoprilabsorption (about 30% as determined byurinaryrecovery) but an increasein exposure(approximately50%) compared to healthy subjects due to decreased clearance.

Renalimpairment

ImpairedrenalfunctiondecreaseseliminationofLisinopril,whichisexcretedviathekidneys,but This decrease becomes clinically important only when the glomerular filtration rate is below 30 ml/min.Inmildtomoderaterenalimpairment(creatinineclearance30-80ml/min)meanAUCwas increased by 13% only, while a 4.5-fold increase in mean AUC was observed in severe renal impairment (creatinine clearance 5-30 ml/min). Lisinopril can be removed by dialysis. During 4 hours of haemodialysis, plasma Lisinopril concentrations decreased on average by 60%, with a dialysis clearance between 40 and 55 ml/min.

Heartfailure

PatientswithheartfailurehaveagreaterexposureofLisinoprilwhencomparedtohealthysubjects (an increase in AUC on average of 125%), but based on the urinary recovery of Lisinopril, there is reduced absorption of approximately 16% compared to healthy subjects.

5.3 **PreclinicalStudy**

Preclinical data reveal no special hazard for humans based on conventional studies of general pharmacology, repeated dose toxicity, genotoxicity, and carcinogenic potential. Angiotensin converting enzyme inhibitors, as a class, have been shown to induce adverse effects on the late foetaldevelopment,resultinginfoetaldeathandcongenitaleffects,inparticularaffectingtheskull.

Foetotoxicity,intrauterinegrowthretardationandpatentductusarteriosushavealsobeenreported. These developmental anomalies are thought to be partly due to a direct action of ACE inhibitors onthefoetalrenin-angiotensinsystemandpartlyduetoischemiaresultingfrommaternal hypotension and decreases in foetal-placental blood flow and oxygen/nutrients delivery to the Foetus.

6. Pharmaceuticalparticulars

6.1 Listofexcipients

Maize Starch, Di Basic Calcium Phosphate Dihydrates, Pregelatinised Starch, Mannitol, Carmellose Sodium, Poly Vinyl Pyrrolidone K-30(PVP K-30), Colour Sunset Yellow Supra, Purified Water, Iso Propyl Alcohol & Magnesium Stearate.

6.2 Incompatibilities

Notapplicable

6.3 Shelflife

36month

6.4 Specialprecautionsforstorage

Storeinattemperaturenotexceeding30°C,inadryplace,Protectfromlight.

6.5 Natureandcontentsofcontainer

14tabletspackedinablister,such02blisterpackedinacartonwithinsert.

6.6 Specialprecautionsfordisposalandotherhandling

Nospecialrequirements.

BRANDNAME:	**RINOSIL10**
GENERICNAME:	**LISINOPRILTABLETSBP10 MG**

7. MarketingAuthorizationHolderMAXH

EALLABORATORIESPVTLTD

PlotNo.-2-7/80-85,Sursez,

G.I.D.C Sachin, Surat,

Gujarat-394230,INDIA.

APPLICANT
Maydon Pharmaceuticals Limited,
Ilupeju, Lagos.

8. MarketingAuthorizationNumber

NotApplicable.

9. DateofFirstAuthorization/RenewaloftheAuthorization

NotApplicable.

10. DateofRevisionoftheText

NotApplicable