ACERIL

RAMIPRIL BP

Compositions:
Aceril 2.5 Tablet: Each film coated tablet contains Ramipril BP 2.5 mg. Aceril 5 Tablet: Each film coated tablet contains Ramipril BP 5 mg.

Pharmacology:
Ramipril and Ramiprilat (active moiety obtained after metabolism by hepatic esterases) inhibit ACE in human subjects and animals. Angiotensin converting enzyme is a peptidyl dipeptidase that catalyzes the conversion of angiotensin I to the vasoconstrictor substance, angiotensin II. Angiotensin II also stimulates aldosterone secretion by the adrenal cortex. Inhibition of ACE results in decreased plasma angiotensin II, which leads to decreased vasopressor activity and decreased aldosterone secretion. The effect of Ramipril on hypertension appears to result at least in part from inhibition of both tissue and circulating ACE activity, thereby reducing angiotensin II formation in tissue and plasma. While the mechanism through which Ramipril lowers blood pressure is believed to be primarily suppression of the renin-angiotensin-aldosterone system, Ramipril has an antihypertensive effect even in patients with low-renin hypertension.

Dosage And Administration:
Hypertension: Initial dose is 2.5 mg to 20 mg once daily. Adjust dosage according to blood pressure response after 2-4 weeks of treatment. The usual maintenance dose following titration is 2.5 mg to 20 mg daily as a single dose or equally divided doses. Reduction in the risk of myocardial infarction, stroke, or death from cardiovascular causes: 2.5 mg once daily for 1 week, 5 mg once daily for 3 weeks, and increased as tolerated to a maintenance dose of 10 mg once daily. Heart failure post-myocardial infarction: Starting dose of 2.5 mg twice daily. If patient becomes hypotensive at this dose, decrease dosage to 1.25 mg twice daily. Increase dose as tolerated toward a target dose of 5 mg twice daily, with dosage increases about 3 weeks apart. Dosage Adjustment: Renal Impairment: Establish baseline renal function in patients initiating Ramipril. Usual regimens of therapy with Ramipril may be followed in patients with estimated creatinine clearance > 40 mL/min. However, in patients with worse impairment, 25% of the usual dose of ramipril is expected to produce full therapeutic levels of ramiprilat. Hypertension: For patients with hypertension and renal impairment, the recommended initial dose is 1.25 mg Ramipril once daily. Dosage may be titrated upward until blood pressure is controlled or to a maximum total daily dose of 5 mg. Heart Failure Post-Myocardial Infarction: For patients with heart failure and renal impairment, the recommended initial dose is 1.25 mg Ramipril once daily. The dose may be increased to 1.25 mg twice daily, and up to a maximum dose of 2.5 mg twice daily depending on clinical response and tolerability. Volume Depletion or Renal Artery Stenosis: Blood pressure decreases associated with any dose of Ramipril depend, in part, on the presence or absence of volume depletion (e.g., past and current diuretic use) or the presence or absence of renal artery stenosis. If such circumstances are suspected to be present, initiate dosing at 1.25 mg once daily. Adjust dosage according to blood pressure response. Geriatric use: No overall differences in effectiveness or safety were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but a greater sensitivity of some older individuals cannot be ruled out

Contraindications:
Ramipril is contraindicated in patients who are hypersensitive to this product or any other ACE inhibitor (e.g., a patient who has experienced angioedema during therapy with any other

ACE inhibitor). Co-administration of aliskiren with Ramipril in patients with diabetes is contraindicated.

Warning And Precaution:
: Angioedema: Use of Ramipril (ACE inhibitors) increase the risk to patients who has the history of angioedema. Hepatic Failure and Impaired Liver Function: Rarely, Ramipril (ACE inhibitors), have been associated with a syndrome that starts with cholestatic 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. Renal impairment: In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with Ramipril (ACE inhibitors) may be associated with oliguria or progressive azotemia and rarely with acute renal failure or death. Treatment of hypertensive patients with Ramipril (ACE inhibitors) having unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine may occur. Neutropenia and Agranulocytosis: In rare instances, treatment with ACE inhibitors may be associated with mild reductions in red blood cell count and hemoglobin 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. Hypotension: Ramipril can cause symptomatic hypotension, after either the initial dose or a later dose when the dosage has been increased. 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. 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. 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. 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).

Side Effects:
The most common adverse reactions in patients with hypertension included headache, dizziness, fatigue, and cough.

Use in Pregnancy and Lactation:
Pregnancy: 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. Lactation: Ingestion of a single 10 mg oral dose of Ramipril resulted in undetectable amounts of Ramipril and its metabolites in breast milk. However, because multiple doses may produce low milk concentrations that are not predictable from a single dose, do not use Ramipril in nursing mothers.

Drug Interaction:
There is possibility of excessive hypotension when Ramipril is used with Diuretics. Use of Lithium with Ramipril serum lithium levels and symptoms of lithium toxicity increases. Nitritoid reactions have been reported when Ramipril is used with Gold. NSAIDS use may lead to increased risk of renal impairment and loss of antihypertensive effect when used with

Ramipril. mTOR inhibitor (e.g. temsirolimus) use with Ramipril may increase angioedema risk.

Overdosage:
Limited data on human overdosage are available. The most likely clinical manifestations would be symptoms attributable to hypotension. Because the hypotensive effect of Ramipril is achieved through vasodilation and effective hypovolemia, it is reasonable to treat Ramipril overdose by infusion of normal saline solution.

Storage:
Store in a cool (below 30°C) and dry place protected from light and moisture. Keep out of the reach of children.

Packing:
Aceril 2.5 Tablet: Each box contains 3×10's tablet in Alu-PVC blister strip. Aceril 5 Tablet: Each box contains 3×10's tablet in Alu-PVC blister strip.

Manufactured By:
The IBN SINA Pharmaceutical Industry PLC.
Shafipur, Gazipur, Bangladesh.