



Ripril®
Ramipril
ACE-Inhibitor

COMPOSITION

Ripril® 1.25 mg capsule : Each capsule contains Ramipril BP 1.25 mg

Ripril® 2.5 mg capsule : Each capsule contains Ramipril BP 2.5 mg

Ripril® 5 mg capsule : Each capsule contains Ramipril BP 5 mg

Ripril® 10 mg capsule : Each capsule contains Ramipril BP 10 mg

PHARMACOLOGY

Ripril® is an angiotensin converting enzyme (ACE) inhibitor. This prodrug itself is a poor inhibitor of ACE but is rapidly hydrolysed after absorption to active metabolite ramiprilat. Following oral administration of ramipril, peak plasma concentration of ramipril is reached within one hour. The extent of absorption is at least 50-60% and is not significantly influenced by the presence of food in the GI tract although the rate of absorption is reduced. Cleavage of the ester group (primarily in the liver) converts ramipril to its active metabolite ramiprilat. Peak plasma concentration of ramiprilat is reached 2-4 hours after drug intake. The serum protein binding of ramipril is about 73% and that of ramiprilat about 56%. Ramipril is almost completely metabolised to ramiprilat, which has about 6 times the ACE inhibitory activity of ramipril. 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. After reaching C_{max}, plasma concentrations decline in a triphasic manner, with the initial rapid decline phase having a half life of 1.1 to 4.5 hours, the apparent elimination phase having a half life of 9-18 hours and the phase involving the dissociation of ramiprilat from ACE and its subsequent elimination having a t_{1/2} of >50 hours.

INDICATION AND USE

1. Mild to severe hypertension, where it may be used alone or in combination with thiazide diuretics
2. Congestive heart failure
3. To reduce the risk of stroke, myocardial infarction and death from cardiovascular events in patients with a history of cardiovascular diseases
4. Proteinuric non-diabetic nephropathy

DOSAGE AND ADMINISTRATION

Dosage of Ripril® must be adjusted according to the patient's tolerance and response.

CARDIOVASCULAR PREPARATIONS

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Hypertension : For the management of hypertension in adults not receiving a diuretic, the usual initial dose of Ramipril is 1.25-2.5 mg once daily. Dosage generally is adjusted no more rapidly than at 2-week intervals. The usual maintenance dosage in adults is 2.5-20 mg daily given as a single dose or in 2 divided doses daily. If BP is not controlled with ramipril alone, a diuretic may be added.

Congestive Heart failure after myocardial infarction : In this case, ramipril therapy may be initiated as early as 2 days after myocardial infarction. An initial dose 2.5 mg twice daily is recommended, but if hypotension occurs, dose should be reduced to 1.25 mg twice daily. Therapy is then titrated to a target daily dose of 5 mg twice daily.

Prevention of major cardiovascular events : In this case, the recommended dose is 2.5 mg twice daily for the first week of therapy and 5 mg once daily for the following 3 weeks; dosage then may be increased, as tolerated, to a maintenance dosage of 10 mg once daily.

Dosage in renal impairment : For the patients with hypertension and renal impairment, the recommended initial dose is 1.25 mg ramipril once daily. Subsequent dosage should be titrated according to individual tolerance and BP response, up to a maximum of 5 mg daily. For the patients with heart failure and renal impairment, the recommended dose is 1.25 mg 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 upon clinical response and tolerability.

CONTRAINDICATION

Ramipril is contraindicated in patients who are hypersensitive to any component of this product and in patients with a history of angioedema related to previous treatment with a ACE inhibitor.

SIDE EFFECT

Ramipril is generally well tolerated. Dizziness, headache, fatigue and asthenia are commonly reported side effects. Other side effects occurring less frequently include symptomatic hypotension, cough, nausea, vomiting, diarrhoea, rash, urticaria, oliguria, anxiety, amnesia, etc. Angioneurotic edema, anaphylactic reactions and hyperkalemia have also been reported rarely.

Warnings : Ramipril should be used with caution in patients with impaired

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renal function, hyperkalemia, hypotension, surgery/anesthesia and impaired hepatic function.

DRUG INTERACTIONS

With Diuretics : Patients on diuretics, especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with ramipril. The possibility of hypotensive effects with ramipril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with ramipril. If this is not possible, the starting dose should be reduced.

With Potassium Supplements and Potassium-sparing Diuretics : Ramipril can attenuate potassium loss caused by thiazide diuretics. Potassium-sparing diuretics (spironolactone, amiloride, triamterene, and others) or potassium supplements can increase the risk of hyperkalemia. Therefore, if concomitant use of such agents is indicated, they should be given with caution, and the patient's serum potassium should be monitored frequently.

With Lithium : Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving ACE inhibitors during therapy with lithium. These drugs should be co-administered with caution, and frequent monitoring of serum lithium levels is recommended. If a diuretic is also used, the risk of lithium toxicity may be increased.

With nonsteroidal anti-inflammatory agents : Rarely, concomitant treatment with ACE inhibitors and nonsteroidal anti-inflammatory agents have been associated with worsening of renal failure and an increase in serum potassium.

Other : Neither ramipril nor its metabolites have been found to interact with food, digoxin, antacid, frusemide, cimetidine, indomethacin, and simvastatin. The combination of ramipril and propranolol showed no adverse effects on dynamic parameters (blood pressure and heart rate). The co-administration of ramipril and warfarin did not adversely affect the anticoagulant effects of the latter drug.

USE IN PREGNANCY

Pregnancy should be excluded before start of treatment with ramipril and avoided during treatment. However, if pregnancy is detected, ramipril should

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be discontinued as early as possible unless continued use is considered life saving.

USE IN LACTATION

Ramipril should not be used during lactation.

USE IN PEDIATRIC PATIENTS

Safety and effectiveness in pediatric patients have not been established.

STORAGE CONDITION

Store at cool & dry place, Protect from light and moisture.

HOW SUPPLIED

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