Angilock®

Losartan Potassium USP

PRESENTATION
Angilock® 25 tablet: Each film-coated tablet contains Losartan Potassium USP 25 mg.
Angilock® 50 tablet: Each film-coated tablet contains Losartan Potassium USP 50 mg.

PHARMACOLOGY
Angiotensin II (formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme) is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiotensin system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Losartan and its principle active metabolite block the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT_1 receptor found in many tissues (e.g. vascular smooth muscle, adrenal gland). There is also an AT_2 receptor found in many tissues but it is not known to be associated with cardiovascular homeostasis. Both Losartan and its principal active metabolite do not exhibit any partial agonist activity at the AT_1 receptor and have much greater affinity (about 1000-fold) for the AT_1 receptor than for the AT_2 receptor. In vitro binding studies indicate that Losartan is a reversible, competitive inhibitor of the AT_1 receptor. Neither Losartan nor its active metabolite inhibits ACE; nor do they bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

PHARMACOKINETICS
Absorption: Following oral administration, losartan is well absorbed, with systemic bioavailability of losartan approximately 33%. Mean peak concentrations of losartan occur at about one hour, and that of its active metabolite at about 3-4 hours.
Distribution: Both losartan and its active metabolite are highly bound to plasma proteins, primarily albumin. The volume of distribution of losartan is about 34 liters, and that of the active metabolite is about 12 liters.
Metabolism: Losartan is an orally active agent that undergoes substantial first-pass metabolism by cytochrome P-450 enzymes. It is converted, in part, to an active carboxylic acid metabolite, that is responsible for most of the angiotensin II receptor antagonism that follows oral losartan administration. Various losartan metabolites have been identified in human plasma and urine. In addition to the active carboxylic acid metabolite, several inactive metabolites are formed.
Excretion: The terminal half-life of losartan itself is about 2 hours, and that of the active metabolite, about 6-9 hours. Both biliary and urinary excretions contribute substantially to the elimination of losartan and its metabolites.

INDICATION
Hypertension: **Angilock®** is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents, including diuretics.
Hypertensive patients with Left Ventricular Hypertrophy: **Angilock®** is indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy.
Nephropathy in Type 2 Diabetic Patients: **Angilock®** is indicated for the treatment of diabetic nephropathy with an elevated serum creatinine and proteinuria (urinary albumin to creatinine ratio ≥300 mg/g) in patients with type 2 diabetes and a history of hypertension.

DOSAGE & ADMINISTRATION
Adult hypertensive patients: The usual starting dose of **Angilock®** is 50 mg once daily. 25 mg used in patients with possible depletion of intravascular volume (e.g., patients treated with diuretics) and patients with a history of hepatic Impairment. **Angilock®** can be administered once or twice daily with total daily doses ranging from 25 mg to 100 mg. The effect of losartan is substantially present within one week but in some studies the maximal effect occurred in 3-6 weeks. No initial dosage adjustment is necessary for elderly patients or for patients with renal impairment, including patients on dialysis. A lower dose should be considered for patients with a history of hepatic impairment. There is no therapeutic experience in patients with severe hepatic impairment. Therefore, losartan is contraindicated in patients with severe hepatic impairment.
Hypertensive patients with Left Ventricular Hypertrophy: The usual starting dose is 50 mg of **Angilock®** once daily. Hydrochlorothiazide 12.5 mg daily should be added and/or the dose of **Angilock®** should be increased to 100 mg once daily followed by an increase in hydrochlorothiazide to 25 mg once daily based on blood pressure response.
Nephropathy in Type 2 Diabetic Patients: The usual starting dose is 50 mg once daily. The dose should be increased to 100 mg once daily based on blood pressure response. **Angilock®** may be administered with insulin and other commonly used hypoglycemic agents (e.g., sulfonylureas, glitazones and glucosidase inhibitors). **Angilock®** may be administered with other antihypertensive agents, and with or without food.
Pediatric hypertensive patients greater than or equal to 6 years of age: The usual recommended starting dose is 0.7 mg/kg once daily (up to 50 mg total) administered as a tablet or a suspension. Dosage should be adjusted according to blood pressure response. Doses above 1.4 mg/kg (or in excess of 100 mg) daily have not been studied in pediatric patients. **Angilock®** is not recommended in pediatric patients less than 6 years of age or in pediatric patients with glomerular filtration rate less than 30 mL/min/1.73 m^2.

CONTRAINDICATION
Losartan is contraindicated in patients who are hypersensitive to any component of this product. Do not co-administer aliskiren with Losartan in patients with diabetes. It is also contraindicated during 2nd and 3rd trimester of pregnancy and in severe hepatic impairment.

SIDE EFFECTS
In controlled clinical trials in patients with essential hypertension, dizziness was the only side effect reported that occurred with an incidence greater than placebo in 1% or more of patients treated with Losartan. Rarely, rash was reported, although the incidence in controlled clinical trials was less than placebo. Angioedema, involving swelling of the face, lips and/or tongue has been reported rarely in patients treated with losartan. Serious hypotension (particularly on initiating treatment in salt-depleted patients) or renal failure (mainly in patients with renal artery stenosis) may be encountered during Losartan treatment.

OVERDOSE
Limited data are available regarding overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia. Bradycardia could occur from parasympathetic (vagal) stimulation. Supportive treatment should include repletion of the intravascular volume. Neither losartan nor the active metabolite can be removed by hemodialysis.

PRECAUTION
In patients who are intravenously volume depleted (e.g. those treated with high-dose diuretics), symptomatic hypotension may occur. These conditions should be corrected prior to the administration of losartan or a lower starting dose should be used. A lower dose should be considered for patients with a history of hepatic impairment. Losartan should not be used with potassium-sparing diuretics.

DRUG INTERACTIONS
No drug interactions of clinical significance have been identified. Compounds which have been studied in clinical pharmacokinetic trials include hydrochlorothiazide, digoxin, warfarin, cimetidine, ketoconazole and phenobarbital.
Serum lithium level should be monitored during concomitant use with losartan. Renal function should be monitored periodically in patients receiving losartan and NSAID therapy. The antihypertensive effect of losartan may be attenuated by NSAIDs, including selective COX-2 inhibitors. Dual blockade of the RAS with angiotensin receptor blockers, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, syncope, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy. Closely monitor blood pressure, renal function, and electrolytes in patients on losartan and other agents that affect the RAS. Do not co-administer aliskiren with losartan in patients with diabetes. Avoid use of aliskiren with losartan in patients with renal impairment (GFR <60 ml/min).

USE IN PREGNANCY & LACTATION
Pregnancy Category D. Although there is no experience with the use of losartan in pregnant women, animal studies with losartan potassium have demonstrated fetal and neonatal injury and death, the mechanism of which is believed to be pharmacologically mediated through effects on the renin-angiotensin-aldosterone system. Losartan should not be used in pregnancy and if pregnancy is detected, losartan should be discontinued as soon as possible. It is not known if losartan is excreted in human breast milk. It is found in rat milk. The drug should not therefore be used in this age group.

STORAGE CONDITION
Store below 30^0 C, protected from light and moisture. Keep out of the reach of children.

HOW SUPPLIED
Angilock® 25 tablet: Box containing 50 tablets in blister pack.
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Manufactured by
SQUARE
PHARMACEUTICALS LTD.
BANGLADESH