

Angilock[®] Plus

Losartan Potassium+Hydrochlorothiazide
Angiotensin Receptor Blocker+Thiazide Diuretic

PRESENTATION

Angilock[®] Plus 50/12.5 Tablet: Each film-coated tablet contains Losartan potassium USP 50 mg + Hydrochlorothiazide BP 12.5 mg.

Angilock[®] Plus 100/25 Tablet: Each film-coated tablet contains Losartan potassium USP 100 mg + Hydrochlorothiazide BP 25 mg.

Angilock[®] Plus 100/12.5 Tablet: Each film-coated tablet contains Losartan potassium USP 100 mg + Hydrochlorothiazide BP 12.5 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 rennin-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 AT1 receptor found in many tissues, (e.g. vascular smooth muscle, adrenal gland). In vitro binding studies indicate that Losartan is reversible, competitive inhibitor of the AT1 receptor. Neither Losartan nor its active metabolite inhibits ACE (kininase II, the enzyme that converts angiotensin I to angiotensin II and degrades bradykinin); nor do they bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

Hydrochlorothiazide is a thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts. Indirectly, the diuretic action of hydrochlorothiazide reduces plasma volume, with consequent increases in plasma renin activity, increases in aldosterone secretion, increases in urinary potassium loss, and decreases in serum potassium. The renin-aldosterone link is mediated by angiotensin II, so coadministration of an angiotensin II receptor antagonist tends to reverse the potassium loss associated with these diuretics.

INDICATIONS AND USES

Management of hypertension.

DOSAGE & ADMINISTRATION

The usual dose of Losartan & Hydrochlorothiazide combination is one tablet of **Angilock[®] Plus 50/12.5** once daily. More than two tablets of **Angilock[®] Plus 50/12.5** once daily or more than one tablet of **Angilock[®] Plus 100/25** once daily is not recommended. The maximal antihypertensive effect is attained about 3 weeks after initiation of therapy. Patient whose blood pressure is not adequately controlled with losartan monotherapy or hydrochlorothiazide alone, may be switched to **Angilock[®] Plus 50/12.5** once daily. If blood pressure remains uncontrolled after about 3 weeks of

therapy, the dose may be increased to two tablets of **Angilock[®] Plus 50/12.5** once daily or one tablet of **Angilock[®] Plus 100/25** once daily. A patient whose blood pressure is not adequately controlled with losartan 100 mg monotherapy may be switched to **Angilock[®] Plus 100/12.5** once daily. If blood pressure remains uncontrolled after about 3 weeks of therapy, the dose may be increased to two tablets of **Angilock[®] Plus 50/12.5** once daily or one tablet of **Angilock[®] Plus 100/25** once daily.

CONTRAINDICATIONS

This combination is contraindicated in patients who are hypersensitive to any component of this product. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

SIDE EFFECTS

Abdominal pain, Edema/swelling, Palpitation, Back pain, Dizziness, Cough, Sinusitis, Upper respiratory infection, Rash.

OVERDOSE

Losartan Potassium:

Limited data are available in regard to overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension occurs, supportive treatment should be instituted. Neither losartan nor its active metabolite can be removed by hemodialysis.

Hydrochlorothiazide:

The most common signs and symptoms observed are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

PRECAUTION

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving thiazide therapy should be observed for clinical signs of fluid or electrolyte imbalance. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy. Because losartan decreases uric acid, losartan in combination with hydrochlorothiazide attenuates the diuretic-induced hyperuricemia. In diabetic patients dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus latent diabetes mellitus may become manifest during thiazide therapy.

DRUG INTERACTION

Losartan potassium:

There is no pharmacokinetic interaction between losartan and hydrochlorothiazide. As with other drugs that block angiotensin II or its effects, concomitant use of potassium-sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium.

Hydrochlorothiazide:

When administered concurrently the following drugs may interact with thiazide diuretics: Alcohol, barbiturates, or narcotics: potentiation of orthostatic hypotension may occur. Antidiabetic drugs (oral agents and insulin): dosage adjustment of the antidiabetic drug may be required. Other antihypertensive drugs additive effect or potentiation: Cholestyramine and colestipol resins: Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins.

USE IN PREGNANCY AND LACTATION

It is not known whether losartan is excreted in human milk, but significant levels of losartan and its active metabolite were shown to be present in rat milk. Thiazides appear in human milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

USE IN PEDIATRIC PATIENTS

The safety and effectiveness in pediatric patients have not been established.

STORAGE CONDITION

Store in a cool and dry place. Protect from light and moisture.

HOW SUPPLIED

Angilock[®] Plus 50/12.5 Tablet: Each box contains 5x10 tablets in blister pack.

Angilock[®] Plus 100/25 Tablet: Each box contains 3x10 tablets in blister pack.

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