Drug Report

Lisinopril

Introduction

Synonyms

mk-521, zestril, prinivil, lisinopril dihydrate, (S)-1-(N(2)-(1-Carboxy-3-phenylpropyl)-L-lysyl)-L-proline, [N2-[(S)-1-CARBOXY-3-phenylpropyl]-L-lysyl-L-proline, Lisinopril, Lisinopril anhydrous, Lisinoprilum

Brand name

AcebitorGlaxoSmithKline, AceminAstraZeneca, AcerbonAstraZeneca, Acinoprilsanofi-aventis, BellisinRanbaxy, BioprilBiochem, DaprilMedochemie, FibsolSigma, FisoprilSanofi-Aventis, HiprilMicro Labs, LinoprilKlinger (Brazil), LisiprilHexal (Czech Republic), Orion (Finland), NopertenDexa (Indonesia), PresitenMagnachem, RanolipRanbaxy, RanoprilRanbaxy, RantexBiotech, SinoprenRanbaxy, SinoprilEczacibasi (Russia), TensoprilMerck

Drug Targets & Associated Pathways what is this?

Lisinopril targets (9 targets)

Show 5 entries Search:

Target(s)	Data Source	Reference(s)	Pathway(s)
ACE	ChEMBL	16784843 16784850	angiotensin | Load in Pathfinder
ACE	DGIdb	24016212 29156001	angiotensin | Load in Pathfinder

		11929321 17618628 9506845	
ACE	DrugBank		angiotensin | Load in Pathfinder
ACE	DGIdb	21804595 29156001	angiotensin | Load in Pathfinder

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Clinical Trials what is this?

Diseases for which Lisinopril is under clinical trial investigation as a treatment (283 Trials)

Provided by ClinicalTrials.gov and the registries and data partners contributing to the OpenTrials project.

Show 5 entries Search:

Disease	Phase	Study Title	Status	Start Date	End Date	Process Date
Glomerulonephritis, IGA	Phase 4	Multicentre Clinical Study to Evaluate the Effect of Personalized Therapy on Patients With Immunoglobulin A Nephropathy. View study report	Not yet recruiting	2022-01-01	2026-12-31	ClinicalTrials.gov processed this data on 2022-09-11

		Immunoglobulin A Nephropathy. View study report				data on 2022-09-11
Nephritis	Phase 4	Multicentre Clinical Study to Evaluate the Effect of Personalized Therapy on Patients With Immunoglobulin A Nephropathy. View study report	Not yet recruiting	2022-01-01	2026-12-31	ClinicalTrials.gov processed this data on 2022-09-11
Glomerulonephritis	Phase 4	Multicentre Clinical Study to Evaluate the Effect of Personalized Therapy on Patients With Immunoglobulin A Nephropathy. View study report	Not yet recruiting	2022-01-01	2026-12-31	ClinicalTrials.gov processed this data on 2022-09-11
Hypertension	Phase 4	Coronavirus (COVID-19) ACEi/ARB Investigation View study report	Suspended	2020-04-30	2021-12-01	ClinicalTrials.gov processed this data on 2022-09-09

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Toxicity Bioassays Tested what is this?

Toxicity endpoints for which Lisinopril has been tested (19 endpoints)

As reported by the FDA

Show 5 entries Search:

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Developmental toxicity in rodent fetus composite	Reproductive and developmental toxicity
Developmental toxicity test in mouse fetus	Reproductive and developmental toxicity
Developmental toxicity test in rabbit fetus	Reproductive and developmental toxicity

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Drug Characteristics what is this?

Characteristics & properties of Lisinopril

Provided by DrugBank

FDA status: small molecule, approved, investigational

Disease Indication: For the treatment of hypertension and symptomatic congestive heart failure. May be used in conjunction with thrombolytic agents, aspirin and/or β-blockers to improve survival in hemodynamically stable individuals following myocardial infarction. May be used to slow the progression of renal disease in hypertensive patients with diabetes mellitus and microalbuminuria or overt nephropathy.

Disease Approval Status:

As reported by ChEMBL and sources cited in the table below:

Show 5 entries Search:

Disease	Status	References
Hypertension	approved	ClinicalTrials FDA
Heart Failure	approved	ClinicalTrials ClinicalTrials FDA
Myocardial Infarction	approved	ClinicalTrials FDA

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Pharmacology: Lisinopril is an orally active ACE inhibitor that antagonizes the effect of the RAAS. The RAAS is a homeostatic mechanism for regulating hemodynamics, water and electrolyte balance. During sympathetic stimulation or when renal blood pressure or blood flow is reduced, renin is released from the granular cells of the juxtaglomerular apparatus in the kidneys. In the blood stream, renin cleaves circulating angiotensinogen to ATI, which is subsequently cleaved to ATII by ACE. ATII increases blood pressure using a number of mechanisms. First, it stimulates the secretion of aldosterone from the adrenal cortex. Aldosterone travels to the distal convoluted tubule (DCT) and collecting tubule of nephrons where it increases sodium and water reabsorption by increasing the number of sodium channels and sodium-potassium ATPases on cell membranes. Second, ATII stimulates the secretion of vasopressin (also known as antidiuretic hormone or ADH) from the posterior pituitary gland. ADH stimulates further water reabsorption from the kidneys via insertion of aquaporin-2 channels on the apical surface of cells of the DCT and collecting tubules. Third, ATII increases blood pressure through direct arterial vasoconstriction. Stimulation of the Type 1 ATII receptor on vascular smooth muscle cells leads to a cascade of events resulting in myocyte contraction and vasoconstriction. In addition to these major effects, ATII induces the thirst response via stimulation of hypothalamic neurons. ACE inhibitors inhibit the rapid conversion of ATI to ATII and antagonize RAAS-induced increases in blood pressure. ACE (also known as kininase II) is also involved in the enzymatic deactivation of bradykinin, a vasodilator. Inhibiting the deactivation of bradykinin increases bradykinin levels and may further sustain the effects of lisinopril by causing increased vasodilation and decreased blood pressure.

Mechanism of Action: There are two isoforms of ACE: the somatic isoform, which exists as a glycoprotein comprised of a single polypeptide chain of 1277; and the testicular isoform, which has a lower molecular mass and is thought to play a role in sperm maturation and binding of sperm to the oviduct epithelium. Somatic ACE has two functionally active domains, N and C, which arise from tandem gene duplication. Although the two domains have high sequence similarity, they play distinct physiological roles. The C-domain is predominantly involved in blood pressure regulation while the N-domain plays a role in hematopoietic stem cell differentiation and proliferation. ACE inhibitors bind to and inhibit the activity of both domains, but have much greater affinity for and inhibitory activity against the C-domain. Lisinopril, one of the few ACE inhibitors that is not a prodrug, competes with ATI for binding to ACE and inhibits and enzymatic proteolysis of ATI to ATII. Decreasing ATII levels in the body decreases blood pressure by inhibiting the pressor effects of ATII as described in the Pharmacology section above. Lisinopril also causes an increase in plasma renin activity likely due to a loss of feedback inhibition mediated by ATII on the release of renin and/or stimulation of reflex mechanisms via baroreceptors.

unaffected by food

Biotransformation: Does not undergo metabolism, excreted unchanged in urine.

Half-life: Effective half life of accumulation following multiple dosing is 12 hours.

Identifiers what is this?

BIOBASE accession: DR000003481

ChEMBL	CHEMBL1237
Drugbank	DB00722
PubChem	5362119