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**Lisinopril** is a drug of the [angiotensin-converting enzyme (ACE) inhibitor](/wiki/ACE_inhibitor) class used primarily in treatment of [high blood pressure](/wiki/Hypertension), [heart failure](/wiki/Heart_failure), and after [heart attacks](/wiki/Myocardial_infarction). It is also used for preventing [kidney](/wiki/Kidney) and [eye](/wiki/Retina) complications in people with [diabetes](/wiki/Diabetes_mellitus). Its indications, [contraindications](/wiki/Contraindication), and side effects are as those for all [ACE inhibitors](/wiki/ACE_inhibitor).

Lisinopril was the third ACE inhibitor (after [captopril](/wiki/Captopril) and [enalapril](/wiki/Enalapril)) and was introduced into therapy in the early 1990s.[[1]](#cite_note-1) A number of properties distinguish it from other ACE inhibitors: It is [hydrophilic](/wiki/Hydrophile), has a long [half-life](/wiki/Half-life) and tissue penetration, and is not [metabolized](/wiki/Metabolism) by the liver.

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## Medical uses[[edit](/index.php?title=(none)&action=edit&section=1)]

Lisinopril is typically used for the treatment of [hypertension](/wiki/Hypertension), [congestive heart failure](/wiki/Congestive_heart_failure), [acute myocardial infarction](/wiki/Acute_myocardial_infarction), and [diabetic nephropathy](/wiki/Diabetic_nephropathy).<ref name=AHFS>[Template:Cite web](/wiki/Template:Cite_web)</ref>

## Contraindications[[edit](/index.php?title=(none)&action=edit&section=2)]

Treatment with lisinopril should be avoided for people who have a history of [angioedema](/wiki/Angioedema) ([hereditary](/wiki/Hereditary) or [idiopathic](/wiki/Idiopathic)) or who have diabetes and are taking [aliskiren](/wiki/Aliskiren).<ref name=Label>[Lisinopril label](http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/019777s073lbl.pdf) Revised: 08/2015</ref>

## Adverse effects[[edit](/index.php?title=(none)&action=edit&section=3)]

[Side effects](/wiki/Adverse_effects), incidence differs depending on which disease state the patient is being treated for.<ref name=Label/>

People taking lisinopril for the treatment of [hypertension](/wiki/Hypertension) may experience the following side effects:

* Headache (3.8%)
* Dizziness (3.5%)
* Cough (2.5%)
* Difficulty swallowing or breathing (signs of [angioedema](/wiki/Angioedema)), [allergic reaction](/wiki/Allergic_reaction) ([anaphylaxis](/wiki/Anaphylaxis))
* [Hyperkalemia](/wiki/Hyperkalemia) (2.2% in adult clinical trials)
* Fatigue (1% or more)
* Diarrhea (1% or more)
* Some severe skin reactions have been reported rarely, including toxic epidermal necrolysis and [Stevens-Johnson syndrome](/wiki/Stevens-Johnson_syndrome); causal relationship has not been established.

People taking lisinopril for the treatment of [acute myocardial infarction](/wiki/Acute_myocardial_infarction) may experience the following side effects:

* [Hypotension](/wiki/Hypotension) (5.3%)
* Renal dysfunction (1.3%)

People taking lisinopril for the treatment of [heart failure](/wiki/Heart_failure) may experience the following side effects:

* [Hypotension](/wiki/Hypotension) (3.8%)
* Dizziness (12% at low dose - 19% at high dose)
* Chest pain (2.1%)
* [Fainting](/wiki/Syncope_(medicine)) (5-7%)
* [Hyperkalemia](/wiki/Hyperkalemia) (3.5% at low dose - 6.4% at high dose)
* Difficulty swallowing or breathing (signs of [angioedema](/wiki/Angioedema)), [allergic reaction](/wiki/Allergic_reaction) ([anaphylaxis](/wiki/Anaphylaxis))
* Fatigue (1% or more)
* Diarrhea (1% or more)
* Some severe skin reactions have been reported rarely, including toxic epidermal necrolysis and [Stevens-Johnson syndrome](/wiki/Stevens-Johnson_syndrome); causal relationship has not been established.

## Special populations[[edit](/index.php?title=(none)&action=edit&section=4)]

Caution should be used in the following populations, as dose adjustments may be required.

### Kidney problems[[edit](/index.php?title=(none)&action=edit&section=5)]

The dose must be adjusted in those with poor kidney function. Dose adjustments may be required when [creatinine clearance](/wiki/Creatinine_clearance) is less than or equal to 30mL/min. Since lisinopril is removed by [dialysis](/wiki/Dialysis), dosing changes must also be considered for people on dialysis.<ref name=Label/>

### Pregnancy and breastfeeding[[edit](/index.php?title=(none)&action=edit&section=6)]

Lisinopril has been assigned to [pregnancy category](/wiki/Pregnancy_category) D by the FDA. Animal and human data have revealed evidence of lethal harm to the embryo and [teratogenicity](/wiki/Teratology) associated with ACE inhibitors. No controlled data in human pregnancy are available. Birth defects have been associated with use of lisinopril in any trimester. However, there have been reports of death and increased toxicities to the fetus and newly born child with the use of lisinopril in the second and third trimesters. The label states, "When pregnancy is detected, discontinue Zestril as soon as possible." The manufacturer recommends mothers should not breastfeed while taking this medication because of the lack of safety data that currently exists.<ref name=Label/> [thumb|Lisinopril 40-mg oral tablet](/wiki/File:003782076lg_Lisinopril_Lisinopril_40_MG_Oral_Tablet.jpg)

## Pharmacology[[edit](/index.php?title=(none)&action=edit&section=7)]

Lisinopril is the [lysine](/wiki/Lysine)-analog of [enalapril](/wiki/Enalapril). Unlike other ACE inhibitors, it is not a [prodrug](/wiki/Prodrug) and is excreted unchanged in the urine. In cases of [overdosage](/wiki/Therapeutic_window), it can be removed from circulation by [dialysis](/wiki/Dialysis).<ref name=Label/>

### Mechanism of action[[edit](/index.php?title=(none)&action=edit&section=8)]

Lisinopril is an [ACE Inhibitor](/wiki/ACE_inhibitor), meaning it blocks the actions of [angiotensin converting enzyme](/wiki/Angiotensin-converting_enzyme) (ACE) in the [renin-angiotensin-aldosterone system](/wiki/Renin–angiotensin_system) (RAAS), keeping [Angiotensin I](/wiki/Angiotensin) from being converted to [Angiotensin II](/wiki/Angiotensin_II). The inhibition of this system causes an overall decrease in blood pressure.[[2]](#cite_note-2)

### Pharmacokinetics[[edit](/index.php?title=(none)&action=edit&section=9)]

The following is a summary of lisinopril's [pharmacokinetics](/wiki/Pharmacokinetics):[[2]](#cite_note-2) **Absorption**

* Lisinopril has a poor [bioavailability](/wiki/Bioavailability) of 25% (Reduced to 16% in people with [NYHA](/wiki/New_York_Heart_Association_Functional_Classification) Class II-IV heart failure)
* Time to peak concentration is 7 hours
* Food has not been shown to affect absorption

**Distribution**

* Does not bind to proteins in the blood
* Lisinopril does not distribute as well in people with NYHA Class II-IV heart failure

**Metabolism**

* Lisinopril does not undergo any form of metabolism in the body

**Elimination**

* Lisinopril leaves the body completely unchanged in the urine
* The [half-life](/wiki/Half-life) of the drug is 12 hours. This is increased in people with kidney problems

## History[[edit](/index.php?title=(none)&action=edit&section=10)]

[Captopril](/wiki/Captopril), the first ACE inhibitor, is a [functional](/wiki/Functional_analog_(chemistry)) and [structural analog](/wiki/Structural_analog) of a [peptide](/wiki/Peptide) derived from the venom of the jararaca, a Brazilian pit viper ([*Bothrops jararaca*](/wiki/Bothrops_jararaca)).<ref name=Patlak>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> [Enalapril](/wiki/Enalapril) is a derivative, designed by scientists at Merck to overcome the rash and bad taste caused by captopril.[[3]](#cite_note-3)<ref name=HistDD>Jie Jack Li, History of Drug Discovery. Chapter 1 in Drug Discovery: Practices, Processes, and Perspectives. Eds. Jie Jack Li, E. J. Corey. John Wiley & Sons, Apr 3, 2013 ISBN 9781118354469</ref>[Template:Rp](/wiki/Template:Rp) Enalapril is actually a [prodrug](/wiki/Prodrug); the active metabolite is [enalaprilat](/wiki/Enalaprilat).<ref name=Menard>Menard J and Patchett A. Angiotensin-Converting Enzyme Inhibitors. Pp 14-76 in Drug Discovery and Design. Volume 56 of Advances in Protein Chemistry. Eds Richards FM, Eisenberg DS, and Kim PS. Series Ed. Scolnick EM. Academic Press, 2001. ISBN 9780080493381. [Pg 30-33](https://books.google.com/books?id=aH6vjC-tXV8C&pg=PA30#v=onepage&q&f=false)</ref>

Scientists at Merck created lisinopril by systematically altering each structural unit of enalaprilat, substituting various amino acids. It turned out that adding [lysine](/wiki/Lysine) at one end of the drug had strong activity and was orally available; analogs of that compounds resulted in lisonopril, which takes its name from the discovery with lysine. Merck conducted clinical trials, and the drug was approved for hypertension in 1987 and congestive heart failure in 1993.<ref name=Menard/>

The discovery posed a problem, since sales of enalapril were strong for Merck, and the company didn't want to diminish those sales. Merck ended up entering into an agreement with [Zeneca](/wiki/Zeneca) under which Zeneca received the right to co-market lisinopril, and Merck received the exclusive rights to an earlier stage [aldose reductase inhibitor](/wiki/Aldose_reductase_inhibitor) drug candidate, a potential treatment for diabetes. Zeneca's marketing and brand name, "Zestril", turned out to be stronger than Merck's effort.[[4]](#cite_note-4) The drug became a blockbuster for [Astrazeneca](/wiki/Astrazeneca) (formed in 1998), with annual sales in 1999 of $1.2B.<ref name=Expirations/>

The US patents expired in 2002.<ref name=Expirations>Express Scripts. [Patent expirations](https://www.express-scripts.com/pharmacist/notifications/docs/genericdrugs.htm)</ref> Since then, lisinopril has been available under many brand names worldwide; some formulations include the [diuretic](/wiki/Diuretic) [hydrochlorothiazide](/wiki/Hydrochlorothiazide).<ref name=Brands>Drugs.com [International brands and formulations for lisinopril](http://www.drugs.com/international/lisinopril.html) Page accessed April 23, 2016</ref>

## See also[[edit](/index.php?title=(none)&action=edit&section=11)]

* [Omapatrilat](/wiki/Omapatrilat)

## References[[edit](/index.php?title=(none)&action=edit&section=12)]

[Template:Reflist](/wiki/Template:Reflist)

## Further reading[[edit](/index.php?title=(none)&action=edit&section=13)]

[Template:Refbegin](/wiki/Template:Refbegin)

* [Template:Cite journal](/wiki/Template:Cite_journal)
* [Template:Cite journal](/wiki/Template:Cite_journal)

[Template:Refend](/wiki/Template:Refend)

## External links[[edit](/index.php?title=(none)&action=edit&section=14)]

* [U.S. National Library of Medicine: Drug Information Portal – Lisinopril](http://druginfo.nlm.nih.gov/drugportal/dpdirect.jsp?name=Lisinopril+anhydrous)

[Template:ACE inhibitors](/wiki/Template:ACE_inhibitors)

[Category:ACE inhibitors](/wiki/Category:ACE_inhibitors) [Category:Carboxamides](/wiki/Category:Carboxamides) [Category:Amino acid derivatives](/wiki/Category:Amino_acid_derivatives) [Category:Carboxylic acids](/wiki/Category:Carboxylic_acids) [Category:Enantiopure drugs](/wiki/Category:Enantiopure_drugs) [Category:Embryotoxicants](/wiki/Category:Embryotoxicants) [Category:Pyrrolidines](/wiki/Category:Pyrrolidines) [Category:Teratogens](/wiki/Category:Teratogens)