Ramipril

	Ramipril			
Trade names	Clinical data	2.5/5/10		
AHFS/Drugs.com	Monograph			
MedlinePlus	a692027			
Pregnancy category	D			
Routes of administration	Oral			
ATC code	С09АА05 (WHO)			
	Legal status			
Legal status	UK: POM (Prescription only) US: R-only			
Pharmacokinetic data				
Bioavailability	28%			
Protein binding	73% (ramipril) 56% (ramiprilat)			
Metabolism	Hepatic, to ramiprilat			
Elimination half-life	2 to 4 hours			

		1
Excretion	Renal (60%) and fecal (40%)	
	Identifiers	
IUPAC name[show]		
CAS Number	87333-19-5 🖌	
PubChem CID	5362129	
IUPHAR/BPS	6339	
DrugBank	DB00178 🖌	
ChemSpider	4514937 🗸	
UNII	L35JN3I7SJ	
KEGG	D00421 - 8	
ChEBI	D00421 ✓ CHEBI:8774 ✓	2.5/5/
ChEMBL	PCHEMBLI 1685/5/10 mg	
ECHA InfoCard	100.170.726 🖉	
	Chemical and physical data	
Formula	$C_{23}H_{32}N_2O_5$	
Molar mass	416.511 g/mol	
3D model (JSmol)	Interactive image	
Melting point	109 °C (228 °F)	
SMILES[show]		
InChI [show]		
	(verify)	

Ramipril, sold under the brand name **Altace** among others, is an angiotensin-converting enzyme (ACE) inhibitor, used to treat high blood pressure (hypertension) and congestive heart failure. By inhibiting an enzyme, ACE inhibitors relax the muscles around small arteries (arterioles). The arterioles expand and allow blood to flow through more easily. This reduces blood pressure.

Medical uses

Indications for its use include:

- High blood pressure
- Congestive heart failure^[1]
- Following heart attack in patients with clinical evidence of heart failure

- Susceptible patients over 55 years: prevention of heart attack, <u>stroke</u>, cardiovascular death, or need of <u>revascularization</u> procedures
- <u>Kidney damage due to diabetes</u> with <u>protein in the urine</u> (In low doses it is used as a prophylaxis for developing nephropathy and related secondary cardiovascular events.)^[2]

Contraindications

Contraindications to its use include renovascular disease (impaired blood flow in the kidneys), severe renal impairment (especially in patients with one kidney or with bilateral <u>renal artery stenosis</u>), volume-depleted patients, a history of <u>angioedema</u> while on an <u>ACE inhibitors</u>, <u>pregnancy</u>, and <u>hypotension</u>.^[Citation needed]

Adverse effects

- Shakiness
- Dry cough
- Dizziness and light-headedness due to low blood pressure
- Fatigue, especially in the early stages
- Mouth dryness in the early stages
- <u>Nausea</u>
- Fainting
- Signs of infection (e.g., fever, chills, persistent sore throat)

Ramipril 2.5 / 5 / 10 mg

- Chest pain
- Neutropenia (low white blood cells)
- Impotence (erectile dysfunction)^[3]

Serious <u>allergic reactions</u> to this drug are unlikely, but immediate medical attention must be sought if they occur. Symptoms of a serious allergic reaction include, but are not limited to a <u>rash</u> or swelling of the face, mouth, tongue, or throat. In extreme cases, ramipril may lead to potentially fatal liver problems.

2.5/5/10

Mechanism of action

See also: Renin-angiotensin system



Ramipril 1.25-mg oral capsule,

letter codes and icons may differ

<u>ACE inhibitors</u> inhibit the actions of <u>angiotensin converting enzyme</u> (ACE), thereby lowering the production of <u>angiotensin II</u> and decreasing the breakdown of <u>bradykinin</u>. The decrease in angiotensin II results in relaxation of <u>arteriole</u> smooth muscle leading to a decrease in <u>total peripheral resistance</u>, reducing blood pressure as the blood is pumped through widened vessels. Its effect on bradykinin is responsible for the dry cough <u>side effect</u>.

Ramipril, a <u>prodrug</u> or precursor drug, is converted to the active <u>metabolite</u> ramiprilat by <u>carboxylesterase</u> <u>1</u>.^[4]E] Ramiprilat is mostly <u>excreted</u> by the <u>kidneys</u>. Its <u>half-life</u> is variable (3–16 hours), and is prolonged by heart and <u>liver failure</u>, as well as <u>kidney failure</u>.

US patent

The compound was protected by the <u>U.S. Patent 5,061,722</u> which was assigned to the German pharmaceutical company <u>Hoechst AG</u> (since merged into <u>Aventis</u>) on 29 October 1991. The patent was scheduled to expire on 29 October 2008. On 11 September 2007, in an appeal by the Indian company <u>Lupin Ltd.</u>, the United States <u>Court of Appeals for the Federal Circuit</u> reversed a district court trial verdict and found that Aventis's patent on ramipril was invalid for "obviousness", opening this drug to generic manufacturers.

Brand names

It is marketed as Prilace by <u>Arrow Pharmaceuticals</u> in <u>Australia</u>, Ramipro by <u>Westfield Pharma</u> in the <u>Philippines</u>, Tritace by <u>Sanofi-Aventis</u> in Italy and United States and Altace by <u>King Pharmaceuticals</u> in the <u>United States</u>, Novapril by Pharmanova in <u>Ghana</u>, Ramitens by PharmaSwiss, Ampril by Krka in Slovenia, Corpril by Cemelog-BRS in Hungary, Piramil and Prilinda by Hemofarm in Serbia, by Lek in Poland and by Novartis and Opsonin Pharma Limited as Ramace in Bangladesh, and in <u>Canada</u> as Altace (Sonfi) and Ramipril (Pharmascience).

Ramipril is marketed in <u>India</u> under the brand names Cardace, Zigpril, Ramistar, Odipril and Zorem . Ramipril is marketed in Myanmar under brand name Endpril .

Clinical trials

The Heart Outcomes and Prevention Evaluation trial[®] seemed to show ramipril possessed cardioprotective qualities which extended beyond its qualities as an antihypertensive. However, the trial and the interpretation of its results have been criticised.[®]

The AIRE trial^{[4][9]} showed a 27% reduction in mortality for patients receiving ramipril for chronic heart failure following a <u>myocardial infarction</u>.

Ramipril was found to have similar results as telmisartan, an angiotensin II receptor blocker.100

References

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- Yusuf S, Teo KK, Pogue J, et al. (April 2008). "Telmisartan, ramipril, or both in patients at high risk for vascular events". N. Engl. J. Med. 358 (15): 1547–59. <u>doi:10.1056/NEJMoa0801317</u>. <u>PMID 18378520</u>.