



# Antihypertensive Summary: Angiotensin-Converting Enzyme(ACE) Inhibitors

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## Angiotensin-Converting Enzyme(ACE) Inhibitors

Drugs included in this group are captopril, enalapril maleate, perindopril tert-butylamine, quinapril, ramipril, trandolapril and Lisinopril. ACE inhibitors are divided into three drug classes.<sup>1,2,3</sup>

Table 1: The classification of ACE inhibitors.

ACE inhibitor Class	Pharmacokinetic distinctions	Examples
Class 1	Readily absorbed ACE inhibitor.	Captopril
Class 2	Inactive pro-drugs, requires liver metabolism for activation.	Enalapril maleate Perindopril tert-butylamine Quinapril Ramipril Trandolapril
Class 3	Active drug , does not require liver metabolism.	Lisinopril

## Mechanism of action of ACE Inhibitors

Angiotensinogen, also referred to as renin substrate, is produced by the liver, while renin is produced by the kidney. Renin converts angiotensinogen into angiotensin-1; angiotensin-converting enzyme (ACE), which is produced by the endothelium of the lung blood vessels, converts angiotensin-1 to angiotensin-2. Angiotensin-2 is a potent vasoconstrictor, which results in increased blood pressure.<sup>4,5,6,7</sup> ACE inhibitors prevent the conversion of angiotensin-1 to angiotensin-2, therefore lowering the blood pressure.

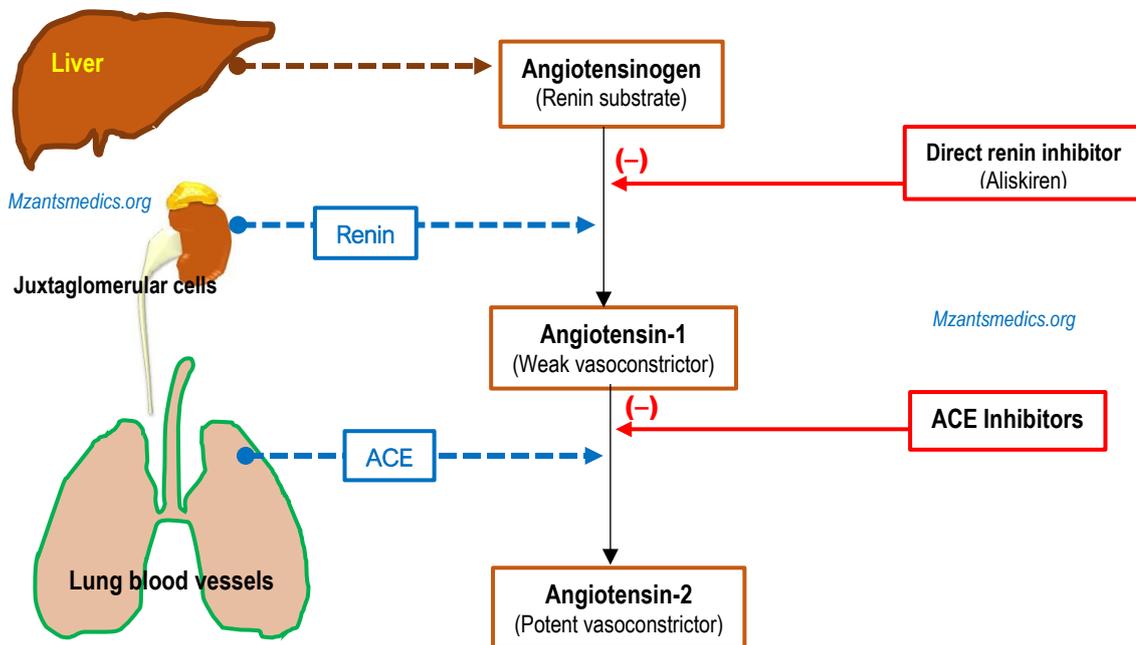


Diagram 1: Mechanism of Action of ACE Inhibitors Mzantsimedics.org

## ACE Inhibitors indications

- Hypertension
- Initiated early, within 24 hours, Post ST Elevation Myocardial Infarction (STEMI).<sup>8,9,10</sup>
- Heart failure<sup>11</sup>
- Diabetes mellitus<sup>12,13</sup>
- Proteinuria or nephrotic syndrome<sup>14,15</sup>
- Chronic kidney disease<sup>16,17</sup>



**ACE INHIBITORS INDICATIONS**

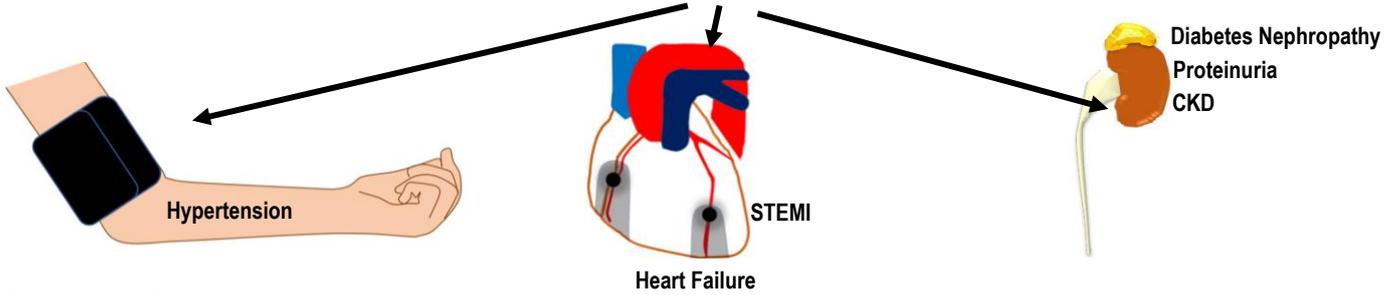


Diagram 2: ACE Inhibitors indications. [Mzantsimedics.org](http://Mzantsimedics.org)

**ACE Inhibitors contraindications**

- Pregnancy<sup>18,19</sup>
- History of angioedema.<sup>20,21</sup>
- Hyperkalemia<sup>22,23</sup>
- Renal artery stenosis<sup>24,25</sup>

**Table 2: ACE inhibitors dosages**

	<b>HYPERTENSION</b>	<b>HEART FAILURE</b>	<b>RENAL IMPAIRMENT (GFR: mL/min)</b>
<b>Captopril</b>	<ul style="list-style-type: none"> <li>• Test dose: 6.25 mg</li> <li>• Initially: 12.5-25 mg B.D.</li> <li>• Increased to: 25 – 50 mg B.D increased at 2-4 week intervals.</li> <li>• Maximum daily dose: 150 mg/day.</li> </ul>	<ul style="list-style-type: none"> <li>• Initially: 6.25 mg t.d.s.</li> <li>• Increased to: 50 mg t.d.s increased at 2-4 week intervals</li> </ul>	<ul style="list-style-type: none"> <li>• <u>GFR 10 – 15</u>: 75% of the dose 12 hourly.</li> <li>• <u>GFR &lt; 10</u>: 50% of the dose every 24 hours.</li> </ul>
<b>Enalapril</b>	<ul style="list-style-type: none"> <li>• 5 – 20 mg O.D.</li> <li>• Divided doses may be given in order to optimize 24-hour blood pressure control</li> </ul>	<ul style="list-style-type: none"> <li>• Initially: 2.5 – 5 mg O.D. under close supervision.</li> <li>• May be increased 10-20 mg B.D.</li> <li>• Maximum daily dose: 40 mg.</li> </ul>	<ul style="list-style-type: none"> <li>• <u>GFR 10 – 50</u>: 50% of the dose.</li> <li>• <u>GFR &lt; 10</u>: 25% of the dose.</li> </ul>
<b>Perindopril</b>	<ul style="list-style-type: none"> <li>• Initial dose: 4 mg O.D.</li> <li>• Maximum: gradually increase to 8 mg O.D.</li> </ul>	<ul style="list-style-type: none"> <li>• Initial dose: 2 mg O.D.</li> <li>• Maximum: gradually increase to 8 mg O.D.</li> </ul>	<ul style="list-style-type: none"> <li>• <u>GFR &lt; 50</u>: 2 mg/24 hours.</li> <li>• <u>GFR 10 – 50</u>: 2 mg/24-48 hours.</li> <li>• <u>GFR &lt; 10</u>: 2 mg/48 hours.</li> </ul>
<b>Quinapril</b>	<ul style="list-style-type: none"> <li>• Initial dose: 10 mg once daily.</li> <li>• Maximum dose: titrate up to 40 mg/day (single or divided doses).</li> </ul>	<ul style="list-style-type: none"> <li>• Initial dose: 2.5 – 5 mg O.D.</li> <li>• Maximum dose: titrate up to 40 mg/day in divided doses.</li> </ul>	<ul style="list-style-type: none"> <li>• <u>GFR 10 – 50</u>: 2.5 – 5 mg/24 hours</li> <li>• <u>GFR &lt; 10</u>: 2.5 mg/24 hours</li> </ul>
<b>Ramipril</b>	<ul style="list-style-type: none"> <li>• Initial dose: 2.5 – 5 mg O.D.</li> <li>• Maximum dose: titrate up to 10 mg O.D.</li> </ul>	<ul style="list-style-type: none"> <li>• Initial dose: 1.25 – 2.5 mg O.D.</li> <li>• Maximum dose: titrate up to 10 mg O.D.</li> </ul>	<ul style="list-style-type: none"> <li>• <u>GFR 10 – 50</u>: 25-50% of the dose.</li> <li>• <u>GFR &lt; 10</u>: 25% of the dose</li> </ul>
<b>Trandolapril</b>	<ul style="list-style-type: none"> <li>• Initial dose: 0.5 – 5 mg O.D.</li> <li>• Maximum dose: titrate up to 4 mg O.D.</li> </ul>	<ul style="list-style-type: none"> <li>• Initial dose: 0.5 – 5 mg O.D.</li> <li>• Maximum dose: titrate up to 4 mg O.D.</li> </ul>	<ul style="list-style-type: none"> <li>• <u>GFR 10 – 50</u>: 50-100% of the dose.</li> <li>• <u>GFR &lt; 10</u>: 50% of the dose</li> </ul>
<b>Lisinopril</b>	<ul style="list-style-type: none"> <li>• Initial dose: 2.5 mg once daily.</li> <li>• Maximum dose: titrate up to 5- 20 mg once daily.</li> </ul>	<ul style="list-style-type: none"> <li>• Initial dose: 2.5 mg once daily.</li> <li>• Maximum dose: titrate up to 20-35 mg once daily.</li> </ul>	<ul style="list-style-type: none"> <li>• <u>GFR: 10 – 50</u>: 50% - 70% of the dose</li> <li>• <u>GFR &lt; 10</u>: 25% - 50% of the dose</li> </ul>



### **ACE inhibitors and the black patient**

Black patients have a higher incidence of low renin hypertension, and therefore ACE inhibitors are less effective in black patients.<sup>26,27,28</sup> Angioedema is also more common in black patients.<sup>29,30,31</sup>

### **Pregnancy and ACE inhibitors**

ACE inhibitors are contraindicated in pregnancy because of their possible teratogenic effects. The decision to stop ACE inhibitors during pregnancy should be taken in consultation with the treating obstetrician.<sup>32,33</sup>

### **Low-salt diet and ACE inhibitors**

A low-salt diet enhances the effects of ACE inhibitors.<sup>34,35</sup>

### **ACE inhibitors side-effects**<sup>36,37,38</sup>

- 1<sup>st</sup> dose hypotension
- Dizziness
- Renal Impairment
- Hyperkalaemia
- Dry irritating cough due to the inhibition of bradykinin degradation
- Angioedema
- Hepatotoxicity
- Skin rashes
- Dysgeusia
- Teratogenic effects in pregnancy

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