Therapeutic Class Overview
Angiotensin-Converting Enzyme (ACE) Inhibitors Single Entity Agents

Therapeutic Class
- **Overview/Summary:** The renin-angiotensin-aldosterone system (RAAS) is the most important component in the homeostatic regulation of blood pressure.\(^1,2\) Excessive activity of the RAAS may lead to hypertension and disorders of fluid and electrolyte imbalance.\(^3\) Renin catalyzes the conversion of angiotensinogen to angiotensin I. Angiotensin I is then cleaved to angiotensin II by angiotensin-converting enzyme (ACE). Angiotensin II may also be generated through other pathways (angiotensin I convertase).\(^1\) Angiotensin II can increase blood pressure by direct vasoconstriction and through actions on the brain and autonomic nervous system.\(^1,3\) In addition, angiotensin II stimulates aldosterone synthesis from the adrenal cortex, leading to sodium and water reabsorption. Angiotensin II exerts other detrimental cardiovascular effects including ventricular hypertrophy, remodeling and myocyte apoptosis.\(^1,2\) The ACE inhibitors block the conversion of angiotensin I to angiotensin II, and also inhibit the breakdown of bradykinin, a potent vasodilator.\(^4\) Evidence-based guidelines recognize the important role that ACE inhibitors play in the treatment of hypertension and other cardiovascular and renal diseases. With the exception of Epaned® (enalapril solution) and Qbrelis® (lisinopril solution), all of the ACE inhibitors are available generically.

<table>
<thead>
<tr>
<th>Generic (Trade Name)</th>
<th>Food and Drug Administration Approved Indications</th>
<th>Dosage Form/Strength</th>
<th>Generic Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benazepril (Lotensin®*)</td>
<td>Hypertension</td>
<td>Tablet: 5 mg, 10 mg, 20 mg, 40 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Captopril*</td>
<td>Diabetic nephropathy, heart failure, hypertension, left ventricular dysfunction post-myocardial infarction</td>
<td>Tablet: 12.5 mg, 25 mg, 50 mg, 100 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Enalapril (Vasotec®, Epaned®)</td>
<td>Asymptomatic left ventricular dysfunction, heart failure, hypertension</td>
<td>Solution: 1 mg/mL, Tablet: 2.5 mg, 5 mg, 10 mg, 20 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Enalaprilat*</td>
<td>Hypertension</td>
<td>Injection: 1.25 mg/mL</td>
<td>✔</td>
</tr>
<tr>
<td>Fosinopril*</td>
<td>Heart failure, hypertension</td>
<td>Tablet: 10 mg, 20 mg, 40 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Lisinopril (Prinivil®, Qbrelis®, Zestril®*)</td>
<td>Acute myocardial infarction to improve survival, heart failure, hypertension</td>
<td>Solution: 1 mg/mL, Tablet: 2.5 mg, 5 mg, 10 mg, 20 mg</td>
<td>✔</td>
</tr>
</tbody>
</table>
### Generic (Trade Name)
- **Moexipril***
- **Perindopril (Aceon®*)
- **Quinapril (Accupril®*)
- **Ramipril (Altace®*)
- **Trandolapril (Mavik®*)

### Food and Drug Administration Approved Indications

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<td>Moexipril*</td>
<td>Hypertension</td>
<td>Table: 7.5 mg, 15 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Perindopril (Aceon®*)</td>
<td>Hypertension, stable coronary artery disease to reduce the risk of cardiovascular mortality or nonfatal myocardial infarction</td>
<td>Tablet: 2 mg, 4 mg, 8 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Quinapril (Accupril®*)</td>
<td>Heart failure, hypertension</td>
<td>Tablet: 5 mg, 10 mg, 20 mg, 40 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Ramipril (Altace®*)</td>
<td>Heart failure post myocardial infarction, hypertension, reduce the risk of myocardial infarction, stroke and death from cardiovascular causes</td>
<td>Capsule: 1.25 mg, 2.5 mg, 5 mg, 10 mg</td>
<td>✔</td>
</tr>
<tr>
<td>Trandolapril (Mavik®*)</td>
<td>Heart failure post-myocardial infarction, hypertension, left ventricular dysfunction post-myocardial infarction</td>
<td>Tablet: 1 mg, 2 mg, 4 mg</td>
<td>✔</td>
</tr>
</tbody>
</table>

*Generic available in at least one dosage form or strength.

### Evidence-based Medicine
- Angiotensin-converting enzyme (ACE) inhibitors have been shown to be effective for coronary artery disease and to reduce the risk of cardiovascular mortality, myocardial infarction and stroke.\(^{19-30}\)
- Clinical Trials have demonstrated the efficacy of ACE inhibitors in reducing mortality associated with congestive heart failure.\(^{31-47}\)
- ACE inhibitors have demonstrated efficacy for the treatment for hypertension and for the use in diabetic nephropathy.\(^{48-79}\)

### Key Points within the Medication Class
- According to Current Clinical Guidelines:\(^{80-97}\)
  - Treatment guidelines for the management of stable angina recommend angiotensin-converting enzyme (ACE) inhibitors in patients with a left ventricular ejection fraction <40% and in those with hypertension, diabetes or chronic kidney disease. ACE inhibitors are also recommended in patients at lower risk (mildly reduced or normal left ventricular ejection fraction) in whom cardiovascular risk factors remain well controlled and revascularization has been performed.
  - Treatment guidelines for the management of unstable angina/non-ST elevation myocardial infarction recommend the use of ACE inhibitors in the first 24 hours in patients with or without pulmonary congestion or left ventricular ejection fraction of <40%. ACE inhibitors are recommended in patients with heart failure, left ventricular dysfunction, diabetes or hypertension. In addition, ACE inhibitors are a reasonable for patients with heart failure and left ventricular ejection fraction >40% and patients without hypertension or diabetes. The guidelines are similar for the management of ST-elevation myocardial infarction.
  - Treatment guidelines recommend ACE inhibitors in patients who are at risk for the development of heart failure. ACE inhibitors are recommended for the management of heart failure in patients who have cardiac structural abnormalities or remodeling who have not
developed heart failure symptoms, especially in patients with reduced left ventricular ejection fraction and a history of myocardial infarction.

- Treatment guidelines for hypertension recommend the use of ACE inhibitors as a first line option in all patients as well as in hypertensive patients with certain compelling indications including heart failure, post-myocardial infarction, left ventricular dysfunction, high coronary disease risk, diabetes, chronic kidney disease, and recurrent stroke prevention.

- Treatment guidelines for the management of hypertension in patients with diabetes recommend a regimen including an ACE inhibitor. In patients with known cardiovascular disease, a regimen including an ACE inhibitor should be used to reduce the risk of cardiovascular events. In patients with type 1 diabetes, with hypertension and any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. In patients with type 2 diabetes, hypertension and microalbuminuria, ACE inhibitors have been shown to delay the progression to macroalbuminuria.

- Other Key Facts:
  - Clinical trials have not demonstrated significant differences when ACE inhibitors were compared to angiotensin II receptor blockers.
  - With the exception of Epaned® (enalapril solution) and Qbrelis® (lisinopril solution), all of the ACE inhibitors are available generically.

References
24. PROGRESS Collaborative group. Randomized trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischemic attack. Lancet. 2001 Sep 29;358(9299):1033-41.


13;348(7):583-92.


