



What Is an Angiotensin Converting Enzyme Inhibitor?

Nancy K. Sweitzer, MD, PhD



Angiotensin converting enzyme inhibitors (ACE inhibitors) are drugs that block the body's production of angiotensin II. Angiotensin II is a hormone that circulates in the blood and has many effects on the cardiovascular system; its main role is to constrict blood vessels. This constriction can cause high blood pressure and increase the work required for the heart to pump blood into the body's main arteries. This causes a problem for the heart muscle if it has been weakened by a heart attack or heart failure. Blocking production of angiotensin II with ACE inhibitors prevents constriction of blood vessels, lowers blood pressure, and lessens the energy the heart has to expend from beat to beat.

In many cardiovascular diseases, angiotensin II is present in abnormally high quantities. The importance of decreasing the damage caused by high levels of angiotensin II is increasingly recognized. ACE inhibitors available in the United States and their associated costs are listed in the Table. The generic names of all ACE inhibitors end with the letters "P-R-I-L" (all drugs have a generic name but may not be available for purchase in a generic form).

In addition to the role it plays in constricting arteries and raising blood pressure, angiotensin II is also "growth-promoting" in a negative way, in that it causes increases in size or thickness of several cardiovascular structures. High levels of circulating angiotensin II lead to thickening of the heart, a condition known as hypertrophy. Hypertrophy of the heart has long been recognized as a marker for high risk of death caused by heart disease. In the presence of high levels of angiotensin II, the walls of blood vessels also become thicker and stiffer, in addition to constricting, and this is thought to predispose to cholesterol deposits and blockages in the arteries, which can lead to heart attacks and strokes. ACE inhibitors are prescribed to prevent or reverse the hypertrophy of the heart and vessel walls. The Figure illustrates the effects of angiotensin II and ACE inhibitors on the cardiovascular system.

Who Should Be Taking an ACE Inhibitor?

Because of their ability to relax constricted blood vessels, ACE inhibitors were first used to lower blood pressure in people with high blood pressure (hypertension). However, there are many other equally effective agents

available to lower blood pressure. Once these drugs had been developed, exciting new possibilities for therapy with ACE inhibitors were recognized. People with weakened heart muscles causing a condition known as heart failure have very high levels of angiotensin II in their blood. It has been established that giving people with heart failure ACE inhibitors delays the onset of symptoms, prevents death from heart failure, and lessens the frequency of hospitalizations. Use of ACE inhibitors was also investigated in people who had had heart attacks but who did not yet have symptoms of heart failure. Again, ACE inhibitors were shown to prevent deaths caused by heart disease in this group. A recent study looked at patients at high risk for having heart attacks or developing heart failure (people with known blockages in arteries, diabetes, or hypertension) and found that treatment with an ACE inhibitor prevented future heart attacks and deaths from heart disease in these groups of people. ACE inhibitors seem to be particularly effective drugs for reducing heart attacks in patients with diabetes. These drugs can also protect kidney function in patients with diabetes and patients with other forms of mild kidney disease, especially those with protein in the urine.

From the Heart Failure Program, University of Wisconsin Hospital and Clinics, Madison, Wis.
Correspondence to Nancy K. Sweitzer, MD, PhD, University of Wisconsin Hospital and Clinics, E5/582 CSC Mail Code 5710, 600 Highland Ave, Madison, WI 53792. E-mail nks@medicine.wisc.edu
(*Circulation*. 2003;108:e16-e18.)

© 2003 American Heart Association, Inc.

Circulation is available at <http://www.circulationaha.org>

DOI: 10.1161/01.CIR.0000075957.16003.07



Who Should Be Taking an ACE Inhibitor?

Patients with:

- Heart failure (weakened heart muscle)
- Coronary artery disease (previous heart attack or angina)
- Adult onset diabetes
- “Diabetic tendency” and high blood pressure
- Mild kidney disease, particularly if there is protein in the urine

Available ACE Inhibitors

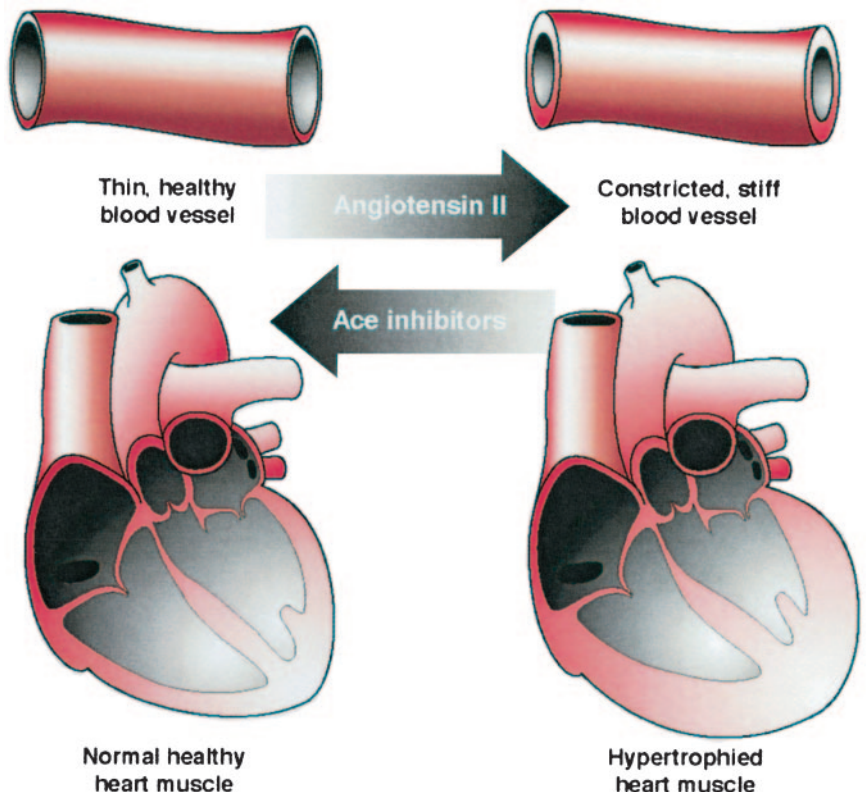
| Generic Name | Trade Names (Manufacturer) | Avail in Generic Form | Approximate Cost for a Month’s Supply |
|--------------|------------------------------------|-----------------------|---------------------------------------|
| Benazepril | Lotensin (Novartis) | no | \$30 |
| Captopril | Capoten (Bristol-Myers Squibb) | yes | \$13 |
| Enalapril | Vasotec (Merck) | yes | \$11 |
| Fosinopril | Monopril (Bristol-Myers Squibb) | no | \$66 |
| Lisinopril | Prinivil (Merck), Zestril (Zeneca) | yes | \$20 |
| Moexipril | Univasc (Schwarz Pharmaceuticals) | no | \$27 |
| Perindopril | Aceon (Solvay Pharmaceuticals) | no | \$43 |
| Quinapril | Accupril (Pfizer) | no | \$32 |
| Ramipril | Altace (Monarch Pharmaceuticals) | no | \$80 |
| Trandolapril | Mavik (Knoll Pharmaceuticals) | no | \$30 |

Are ACE Inhibitors Safe?

ACE inhibitors are taken by thousands of patients and have been shown to be very safe. However, all medications have side effects, and there are some for which patients should be monitored. Because ACE inhibitors can lower blood pressure, lightheadedness and dizziness may result if blood pressure becomes too low. As ACE inhibitors reduce blood pressure only modestly in most patients, this is not a major problem, particularly if the initial dose is low. Oddly enough, the major side effect of ACE inhibitors is a cough. The cough occurs in about 15% of patients; however, it is mild in half of these patients and does not require stoppage of the drug. About 8% of patients have a cough bothersome enough that ACE inhibitor therapy has to be discontinued. Finally, ACE inhibitors can worsen kidney function in some patients, particularly if cholesterol buildup is blocking the arteries to both kidneys. However, long-term therapy with ACE inhibitors has been shown to prevent worsening of kidney function in patients with mild kidney disease due to diabetes or high blood pressure. If you have abnormal kidney function, ask your doctor for more information.

called angioedema as a result of their first dose of an ACE inhibitor. Once this reaction occurs, ACE inhibitors should never be used again. Any person who has ever had a swelling reaction like this in any situation, such as after a bee sting or eating nuts, should avoid all ACE inhibitors.

Because they have been associated with birth defects, ACE inhibitors are not safe during pregnancy. If you have cardiovascular disease treated with an ACE inhibitor and are or are thinking about becoming pregnant, contact your doctor immediately. These drugs are also not advised for use by nursing mothers.



Effects of angiotensin II on the blood vessels and heart.

Are There People Who Should Not Take ACE Inhibitors?

About 1 in 100 patients have a severe throat and tongue swelling reaction

Will an ACE Inhibitor Interact With My Other Medications?

ACE inhibitors are very safe and can be used in combination with almost any other medication. Other drugs that affect the kidneys, such as furosemide (Lasix) or hydrochlorothiazide should be used with caution, and kidney function should be monitored. In patients taking insulin, starting an ACE inhibitor may be associated with a fall in blood sugar to low levels, and sugars should be watched closely the first few days on the drug. Finally, some over-the-counter pain medication such as

ibuprofen (for example, Advil, Motrin), naprosyn (Aleve), and other related compounds can make ACE inhibitors less effective and should be avoided. Acetaminophen (Tylenol) can be taken with ACE inhibitors. Review your medication use, including over-the-counter medications, with your doctor before beginning to take ACE inhibitors.

Additional Resources

Bicket DP. Using ACE inhibitors appropriately. *Am Fam Physician*. 2002;66:461–468.
National Library of Medicine. MEDLINE plus health information. Available at: <http://www.nlm.nih.gov/medlineplus/>. Accessed June 23, 2003.

WebMDHealth web site. Available at: <http://my.webmd.com>. Accessed June 23, 2003.
National Library of Medicine. Health information. Available at: <http://www.nlm.nih.gov/hinfo.html>. Accessed June 23, 2003.
National Institute of Diabetes and Digestive and Kidney Disease web site. Available at: <http://www.niddk.nih.gov>. Accessed June 23, 2003.
Cardio Info Innovations. Cardiology patient info. Available at: <http://cardio-info.com/lnkpinfo.htm>. Accessed June 23, 2003.
CHFpatients.com web site. Available at: <http://www.chfpatients.com>. Accessed June 23, 2003.
Heart Failure Society of America. Heart failure information and education. Available at: <http://www.abouthf.org>. Accessed June 23, 2003.