

# Consumer Reports BEST BUY DRUGS™

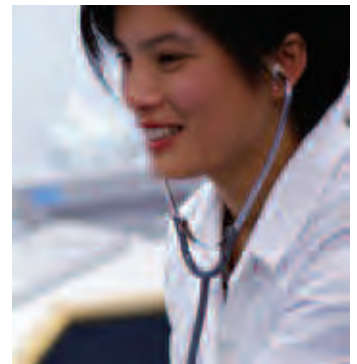
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Treating High Blood Pressure and Heart Disease:

## The ACE Inhibitors

Comparing Effectiveness, Safety, and Price



## Our Recommendations

ACE Inhibitors (ACEIs) are used by tens of millions of Americans to treat high blood pressure, heart failure, diabetes, and kidney disease.

The cost for ACEIs varies from about \$20 to more than \$100 a month. This report gives you information that could save you hundreds of dollars a year if you are currently taking a brand-name ACEI, and \$1,200 or more a year if you are taking the highest-priced ACEIs.

ACEIs are effective, life-saving medicines with more than 20 years of widespread safe use. They help lower the risk of both fatal and nonfatal heart attacks and strokes, and kidney failure. And they improve quality of life. This report compares the effectiveness, safety, and cost of the 10 ACEIs.

We have selected the following five ACEIs as *Consumer Reports Best Buy Drugs* based primarily on the evidence for their effectiveness, but also on dosing convenience and cost in treating the following conditions:

- *For high blood pressure:* benazepril, enalapril, and lisinopril
- *For heart failure:* enalapril, captopril
- *After a heart attack:* lisinopril
- *For diabetics:* ramipril (Altace)
- *For people with kidney disease:* benazepril, ramipril (Altace)

Four of these medicines are low-cost or moderately priced generics. All have been proven to be just as effective as or *superior* to other ACEIs. One *Best Buy* – ramipril (Altace) – is a brand-name drug for which no generic copy is yet available. Altace is moderately priced.

The ACEIs can lower blood pressure. But they should not be taken as initial “first-step” treatment by people with high blood pressure who do not have heart disease, diabetes, or kidney disease.

# Welcome

This report on a class of drugs called ACE Inhibitors (ACEIs) is part of a Consumers Union and *Consumer Reports* project to help you find safe, effective medicines that give you the most value for your health-care dollar. To learn more about the project and other drugs we've evaluated, go to [www.CRBestBuyDrugs.org](http://www.CRBestBuyDrugs.org).


ACEIs are used by millions of people everyday. (ACE stands for angiotensin-converting enzyme.) They were the third most widely prescribed class of medicines in 2004, and are used primarily to treat people who have high blood pressure and/or heart failure (also called congestive heart failure). Heart failure occurs when the heart muscle weakens, limiting the heart's ability to pump blood. Despite its name, heart failure is usually a chronic disease that can worsen over time and occurs as a result of untreated or inadequately controlled high blood pressure, a heart attack, or a number of diseases that attack the heart muscle. (See Table 1 on page 6.)

The ACEIs are also widely used to treat people after a heart attack (in the absence of heart failure) and people with diabetes with and without kidney disease.

Ten ACEIs are currently approved for use in the United States. Seven are now available as generic drugs and three are not (indicated by \* below). Some of the generic ACEIs are very inexpensive, costing about \$10 to \$20 a month. (See Table 4 on pages 12-14.) The 10 drugs are:

Generic Name	Brand Name(s)
Benazepril	Lotensin
Captopril	Capoten
Enalapril	Vasotec
Fosinopril	Monopril
Lisinopril	Prinivil, Zestril
Moexipril	Univasc
Perindopril*	Aceon
Quinapril	Accupril
Ramipril*	Altace
Trandolapril*	Mavik

\* Sold only by the brand-name. Not yet available as a generic.



ACEIs are just one class of prescription medicine used to treat high blood pressure, heart failure and other heart-related ailments. Four other classes are commonly used to treat high blood pressure, for example. Those include beta-blockers, calcium-channel blockers, diuretics, and angiotensin-receptor blockers. Those four plus ACEIs are often used in various combinations. Indeed, many people with high blood pressure will have to take two or more drugs to bring their blood pressure down to normal. Heart failure is also routinely treated with multiple drugs.

Talk with your doctor about the right mix of blood pressure and heart medicines for you, as well as lifestyle changes – such as healthy diet, weight loss, exercise, controlling alcohol use, and quitting smoking – that could reduce your need for medicines and help preserve your health.

You should know that high blood pressure in particular is one of the most significantly under-diagnosed and under-treated diseases in the U.S., in part because it usually has no symptoms. It raises your risk of heart attack, heart failure, stroke, dementia, vision loss, and kidney failure. In most who have it, it is a lifelong condition. Estimates vary, but at least 65 million Americans – including a third of adults aged 18 and over – have high blood pressure. Yet studies show that:

- 30% are *unaware* of their condition and not getting any treatment
- 15% are aware of their condition but not getting treatment or taking medicine
- 25% are getting treatment but their high blood pressure is *not* under control

That leaves only 30% of people with high blood pressure getting the medicines, care and blood pressure control they need. Uncontrolled high blood pressure is a leading cause of death. In addition, high blood pressure's dangers are thought to extend to an additional *45 to 60 million* Americans who have “prehypertension,” or borderline high blood pressure. (See Table 2 on page 8.)

The upshot: you should have your blood pressure checked frequently – at least once a year, more often if you are over age 50, and *every time* you visit a doctor. High blood pressure can occur at any age but is far more common in people aged 35 and over and among African-Americans.

Heart failure is also under-diagnosed and under-treated, especially in its early stages. People often assume its symptoms are a sign of normal aging,

or just not serious. And doctors can sometimes misdiagnose these symptoms, which include shortness of breath on exertion, unexplained coughing or wheezing, and ankle swelling.

This report is based on a comprehensive expert analysis of the medical evidence on ACEIs. There's more information on page 18 and at [www.CRBestBuyDrugs.org](http://www.CRBestBuyDrugs.org) about how we conducted our evaluation.

*This report was released and last updated in April 2005*

*Note to Readers: This is the second of three sequential reports on prescription medicines to treat high blood pressure and other heart conditions. A report on beta-blockers was released in March. Next month's report, in May, will focus on a class of drugs called Calcium Channel Blockers. In addition, we will soon post a separate report to help you make sense of all the types of drugs used – often in combination – to treat high blood pressure. Sign up for an e-mail alert at [www.CRBestBuyDrugs.org](http://www.CRBestBuyDrugs.org) if you'd like us to tell you when these reports will be posted.*



## What Are ACEIs and Who Needs Them?

ACEIs work by blocking an enzyme that leads to the release of a substance called angiotensin, which causes blood vessels to constrict. Thus, ACEIs relax blood vessels throughout the body, lowering blood pressure and reducing the workload on the heart.

ACEIs are not the best initial choice for many people with high blood pressure. Recent studies indicate that inexpensive generic diuretics (often called water pills) are a better first choice, especially for people who have high blood pressure but no other heart problems or diabetes. Those studies show that diuretics can prevent heart attacks, heart failure, strokes, and deaths as effectively as ACEIs or other classes of high blood pressure drugs.

Some people who are already taking a diuretic, however, and need a second drug to lower their blood pressure can benefit from taking an ACEI. If you fall

in this category – needing a second blood pressure-lowering drug – your doctor will be weighing the relative merits of giving you an ACEI, a beta-blocker or another type of drug, based on your individual medical circumstances.

ACEIs are usually or often a *first choice*, however, if you have one or more of the following conditions, with or without high blood pressure:

- Heart failure
- Heart attack (myocardial infarction) or stroke in the past
- Diabetes
- Diabetic kidney disease

In particular, ACEIs have become a cornerstone of treatment for heart failure. They effectively – some-

**Table 1. Heart Failure – Types, Symptoms, and Tests**

Two Types	Symptoms and Tests
<p><b>Systolic heart failure</b> occurs when the heart cannot contract forcefully enough to push enough blood into circulation.</p> <p><b>Diastolic heart failure</b> occurs when the heart's pumping chambers have become too stiff, preventing them from filling with enough blood before the heart contracts to push the blood into circulation.</p> <p><b>In both types</b>, blood coming into the left chamber from the lungs can "back up," causing fluid to leak into the lungs. This condition is called pulmonary edema. Heart failure can also cause fluid build-up elsewhere in the body. Doctors refer to this as edema.</p> <p><b>Heart failure</b> (both types) occurs over time, with the heart losing its pumping capacity bit by bit over years. Thus, it is a chronic disease. The heart compensates at first – by enlarging or pumping faster, for example. This can mask the condition. But over time, the heart loses its capacity to compensate, and symptoms develop.</p>	<ul style="list-style-type: none"> <li>■ Fatigue</li> <li>■ Shortness of breath on exertion</li> <li>■ Difficulty breathing</li> <li>■ Wheezing</li> <li>■ Frequent coughing (especially at night)</li> <li>■ Swollen ankles</li> <li>■ Unexplained weight gain</li> <li>■ Bulging neck veins</li> </ul> <p>Ask your doctor to check for heart failure if you have any of these symptoms and they cannot be explained by other causes.</p> <p>A test called an echocardiogram measures the pumping capacity of the heart and can detect thickening of the wall of the heart and heart failure.</p>

Sources: *Guide to a Healthy Heart*, Consumer Reports on Health, Consumers Union, (2003); American Heart Association

times dramatically – slow the progression of the condition. Selected ACEIs are also now commonly used in people whose kidneys are failing due to diabetes. Indeed, evidence is emerging that ACEIs may prevent the decline of kidney function in people with diabetes and should be routinely prescribed for most diabetics.

People who have one or more of the conditions listed on page 6 may also benefit from taking a beta-blocker in addition to an ACEI. Both classes of drugs have been proven to be protective to the heart, and they can act together to lower your risk of a heart attack or stroke, or death. Our beta-blocker report can be obtained at [www.CRBESTBUYDRUGS.org](http://www.CRBESTBUYDRUGS.org).

## The Basics on High Blood Pressure

Americans' health could be markedly improved if they were more alert to the dangers of high blood pressure and the need to have their blood pressure checked regularly.

Blood pressure is the force in the arteries when blood is pumped out of the heart. It's measured in millimeters of mercury (abbreviated as mm Hg) and the measurement consists of two numbers. One number, usually given first, is the pressure when the heart beats; that's called the systolic pressure. The second number is the pressure when the heart is at rest. That's called the diastolic pressure. Both matter. Your doctor may say or present them, for example, as "120 over 80" or 120/80 mm Hg.

High blood pressure – the causes of which are not well understood – is defined, for adults, as a systolic pressure of 140mm Hg or greater and/or a diastolic pressure of 90mm Hg or greater. Normal blood pressure is defined as a systolic reading of less than 120mm Hg and a diastolic reading of less than 80mm Hg.

That leaves a gap between "normal" and "high." That gap is now labeled "prehypertensive." Based on recent studies, if your blood pressure readings fall in that gap, you are at risk of developing high blood pressure and already have some elevated risk of heart disease and stroke. You need to get your blood pressure down. Table 2 on the next page presents these levels of blood pressure and general treatment guidance. If your blood pressure levels are prehypertensive and you have heart or kidney disease or diabetes, you may need drug treatment to lower your blood pressure.

Note: Both numbers – systolic and diastolic – don't have to be high at the same time, and often are not. Even if one is elevated, you are considered to have high blood pressure. Indeed, in people aged 50 and over, a high systolic reading appears to be much more strongly linked to a higher risk of heart disease and heart attack than a high diastolic blood pressure.

High blood pressure's relationship to stress, anxiety, nervousness, or feeling tense is often misunderstood. Feeling excited, anxious, or fearful can indeed raise blood pressure, but usually only temporarily – due to the surge of adrenaline that often accompanies these feelings. But those are *not* symptoms of high blood pressure. You can be a calm, relaxed person who never gets anxious or fearful and still have high blood pressure. And you will have no symptoms. The only way to detect your high blood pressure is to have it checked regularly using a blood pressure arm cuff.



**Table 2. Blood Pressure Levels and Treatment Guidance**

Blood Pressure Classification	Systolic Measure (mm Hg)	Diastolic Measure (mm Hg)	General Treatment Guidance
Normal	Below 120	Below 80	<ul style="list-style-type: none"> <li>■ No treatment needed</li> <li>■ Healthy lifestyle encouraged to maintain normal blood pressure</li> </ul>
Prehypertensive	120-139	80-89	<ul style="list-style-type: none"> <li>■ Lifestyle changes needed: weight loss, quitting smoking, low-salt and low-fat diet, moderate alcohol use, and increased exercise</li> <li>■ Drug treatment not indicated except if you have diabetes, kidney or heart disease</li> </ul>
Stage 1 High Blood Pressure	140-159	90-99	<ul style="list-style-type: none"> <li>■ Lifestyle changes urged, same as above</li> <li>■ Drug treatment needed. Doctor may start with one medicine to see if it does the job.</li> </ul>
Stage 2 High Blood Pressure	160 or above	100 or above	<ul style="list-style-type: none"> <li>■ Lifestyle changes urged, same as above</li> <li>■ Drug treatment needed. Two or more medicines usually required to bring blood pressure down.</li> </ul>

Source: Chobanian AV, Bakris GL, Black HR, et al., "The seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure," *Journal of the American Medical Association*, 2003; 289(19):2560-2572

## Choosing an ACEI – Our *Best Buy* Picks

Choosing an ACEI depends on what you need it for. Studies show that some ACEIs are more effective and safer than others for certain conditions. If you have two or more of the medical conditions we discuss below, or others, your doctor will be making a judgment about which ACEI and dose is best for you.

The information in this report will help you talk to your doctor about which ACEI is right for you, and which may cost you the least money out-of-pocket.

People respond to the various ACEIs differently. So you may have to try more than one if your doctor judges that the one you were initially prescribed is not working well. In addition, ACEIs can have side effects, and you may respond to one better than another. Side effects include fatigue, weakness, dizziness, a persistent dry cough, potassium imbalance, and a condition called angioedema. Angioedema – facial swelling that can close off the wind pipe – is rare but can be life-threatening. It is more common in African-Americans.

Starting with as low a dose of an ACEI as possible can reduce the risk of side effects. That is especially a factor for people with heart failure, who often are prescribed higher doses of ACEIs. If the side effects persist, you may want to talk with your doctor about trying a different ACEI.

You and your doctor should be choosing an ACEI based primarily on its record in reducing heart attacks, strokes, and preventing the progression of heart disease and failure, coronary artery disease, and kidney disease. Where the evidence is equivocal, cost may be a deciding factor, especially if you have no drug coverage. The ACEIs vary in cost from \$15 to \$50 for most generics to more than \$100 for many brand-name versions.

For many people, the convenience of once-a-day dosing also may be important. An advantage in using a drug that has been proven to prevent serious events – such as heart attacks, strokes, and death from one of these causes – is that your doctor will (or should) know what dose of the drug has been shown to save lives.

Ramipril (Altace) and captopril (Capoten) have the strongest evidence of effectiveness across various medical conditions. But several other ACEIs have been proven to preserve health and reduce deaths in at least one condition. (See Table 3 on page 10). Evidence is more limited for fosinopril (Monopril), moexipril (Univasc), perindopril (Aceaon), and quinapril (Accupril).

Taking effectiveness, safety, dosing convenience, and cost into account, we have selected the following ACEIs (at all doses listed) as *Consumer Reports Best Buy Drugs* for these medical conditions:

- *For high blood pressure:* benazepril, enalapril, and lisinopril
- *For heart failure:* enalapril, captopril
- *After a heart attack:* lisinopril
- *For diabetics:* ramipril (Altace)
- *For people with kidney disease:* benazepril, ramipril (Altace),

Four of these medicines are low-cost or moderately priced generics. All have been proven to be just as effective or *superior* to other ACEIs. There is no reason to take the brand-name versions of these medicines. One *Best Buy* – ramipril (Altace) – is a brand-name drug for which no generic copy is yet available. Altace is a moderately priced medicine. Studies have proven it particularly effective in treating people who have diabetes and other heart disease risk factors, and in preventing kidney decline among diabetics.

*Treating high blood pressure.* All 10 ACEIs are approved by the FDA for treating high blood pressure. All are effective for this purpose; studies do not indicate that any one ACEI is better than any other in lowering blood pressure.

As mentioned earlier, ACEIs are *not* indicated as a first line treatment for people with high blood pressure alone. They are prescribed frequently as a sec-

ond drug for people who have highly elevated blood pressure or whose blood pressure has failed to be lowered by a single drug. No studies indicate that any ACEI is better for that than any other.

Thus, if you have high blood pressure but no other heart condition, any ACEI can help when used in combination with another class of high blood pressure drug (such as a diuretic).

Our choice of three *Best Buy* ACEIs for high blood pressure – benazepril, enalapril, and lisinopril – is

based on cost and dosing convenience. All are relatively low-cost generics and need to be taken just once a day. There is no reason to take the more expensive brand-name version of any of these medicines, other brand-name ACEIs, or the somewhat more expensive generic options.

*Treating heart failure.* Evidence supports seven ACEIs in the treatment of heart failure, with the strongest evidence for four. (See Table 3.) No studies indicate a clear advantage for one or more of these four – captopril, enalapril, ramipril and trandolapril – in slow-

**Table 3. Summary of Evidence on the Effectiveness of the ACEIs**

Drug (Generic Name)	People With Heart Failure		People Who Have Had a Heart Attack	People Who Have Diabetes and Other Heart Risk Factors		People With Kidney Disease	
	Reduce Deaths	Improve Quality of Life	Reduce Deaths	Reduce Risk of Heart Attack or Stroke	Reduce Deaths	Reduce Risk of Heart Attack or Stroke	Prevent Decline in Kidney Function, Kidney Failure, and/or Reduce Deaths
Benazepril	+						++
Captopril	++	++	++	++			++
Enalapril	++	++		+		++	
Fosinopril		++					
Lisinopril	+	++	++	++			
Moexipril							
Perindopril			0	++	0		
Quinapril					0		++
Ramipril	++	++	++	++	++	++	++
Trandolapril	++	++	++	++			

++ Good evidence for effectiveness  
+ Probably Effective

0 Probably not effective  
Empty square = no evidence one way or the other

ing the progression of heart failure or improving the quality of life. On the basis of cost and dosing convenience, we have chosen generic **enalapril** as the *Best Buy* drug for people with early or mild heart failure. This drug costs \$18 to \$23 per month for the one-a-day dose.

As indicated above, people with heart failure, especially as it worsens, may require higher doses or multiple daily doses of an ACEI. Enalapril is frequently prescribed at higher doses and is still a good value at twice daily dosing. But captopril has an advantage for some people with heart failure. It has a quick onset and short duration of action; this benefits frail patients with more severe heart failure. It's also why captopril needs to be taken three times a day. The \$31 to \$55 per month cost for three daily doses is a good value for such patients. For that reason we have chosen **captopril** as a *Best Buy* for people who need more frequent dosing.

*After a heart attack.* Evidence supports four ACEIs in the treatment of people after a heart attack – captopril, lisinopril, ramipril, and trandolapril. All help lower the risk of a repeat heart attack, heart failure, and death. Based on the studies to date, none of these four seems to have a clear advantage over the others in either effectiveness or safety.

Taking cost and doing convenience into account, we have chosen generic **lisinopril** as the *Best Buy* drug for most people who need an ACEI after a heart attack.

*For diabetics.* Studies show that five ACEIs are effective at substantially lowering the risk of heart attacks and strokes in people with diabetes. (See Table 3.) Most studies have been done in people who also have other risk factors for heart disease as well as diabetes – such as elevated cholesterol, being a smoker or being overweight.

But only one ACEI – **ramipril (Altace)** – has been shown so far to reduce premature deaths among diabetics who have other heart disease risk factors. Ramipril is available only as brand-name Altace. Despite its higher cost (\$50 to \$65 a month) relative to most other ACEIs, we have chosen it as a *Best Buy*












drug for diabetics because of this demonstrated superior effectiveness.

*Treating kidney disease:* Studies show that five ACEIs are effective at preventing a decline in kidney function or lowering the risk of heart disease or stroke, or both. All are acceptable choices. The strongest evidence is for benazepril, captopril, and ramipril (Altace), however.





On this basis, and taking dosing convenience and cost into consideration, we have chosen generic **benazepril** as the *Best Buy* drug for people with declining kidney function who do not have diabetes. **Ramipril (Altace)** is the preferred drug and *Best Buy* for people with diabetes who have declining kidney function, as indicated above.







**Table 4. ACEI Cost Comparison and Best Buy Indication**

	Generic Name and Dose	Brand Name <sup>1</sup>	Frequency of Use (per day)	Average Monthly Cost <sup>2</sup>	Best Buy Indication
	Benazepril 10mg	Lotensin	One	\$43	
	Benazepril 10mg	Generic	One	\$22	High Blood Pressure, Kidney Disease
	Benazepril 20mg	Lotensin	One	\$43	
	Benazepril 20mg	Generic	One	\$22	High Blood Pressure, Kidney Disease
	Benazepril 40mg	Lotensin	One	\$44	
	Benazepril 40mg	Generic	One	\$22	High Blood Pressure, Kidney Disease
	Captopril 12.5mg	Capoten	Three	\$133	
	Captopril 12.5mg	Generic	Three	\$30	Heart Failure
	Captopril 25mg	Capoten	Three	\$131	
	Captopril 25mg	Generic	Three	\$31	Heart Failure
	Captopril 50mg	Capoten	Three	\$220	
	Captopril 50mg	Generic	Three	\$44	Heart Failure
	Captopril 100mg	Capoten	Three	\$271	
	Captopril 100mg	Generic	Three	\$55	Heart Failure
	Enalapril 5mg	Vasotec	One	\$39	
	Enalapril 5mg	Generic	One	\$18	High Blood Pressure, Heart Failure
	Enalapril 10mg	Vasotec	One	\$40	
	Enalapril 10mg	Generic	One	\$19	High Blood Pressure, Heart Failure
	Enalapril 20mg	Vasotec	One	\$56	
	Enalapril 20mg	Generic	One	\$23	High Blood Pressure, Heart Failure
	Enalapril 20mg	Vasotec	Two	\$111	
	Enalapril 20mg	Generic	Two	\$46	High Blood Pressure, Heart Failure
	Fosinopril 10mg	Monopril	One	\$47	
	Fosinopril 10mg	Generic	One	\$35	

**Table 4. ACEI Cost Comparison and Best Buy Indication**

Generic Name and Dose	Brand Name <sup>1</sup>	Frequency of Use (per day)	Average Monthly Cost <sup>2</sup>	Best Buy Indication
Fosinopril 20mg	Monopril	One	\$47	
Fosinopril 20mg	Generic	One	\$34	
Fosinopril 40mg	Monopril	One	\$47	
Fosinopril 40mg	Generic	One	\$35	
Lisinopril 10mg	Prinivil	One	\$38	
Lisinopril 10mg	Zestril	One	\$40	
 Lisinopril 10mg	Generic	One	\$18	After a Heart Attack
Lisinopril 20mg	Prinivil	One	\$41	
Lisinopril 20mg	Zestril	One	\$44	
 Lisinopril 20mg	Generic	One	\$20	After a Heart Attack
Lisinopril 30mg	Zestril	One	\$59	
 Lisinopril 30mg	Generic	One	\$26	After a Heart Attack
Lisinopril 40mg	Prinivil	One	\$59	
Lisinopril 40mg	Zestril	One	\$61	
 Lisinopril 40mg	Generic	One	\$27	After a Heart Attack
Moexipril 7.5mg	Univasc	One	\$46	
Moexipril 7.5mg	Generic	One	\$30	
Moexipril 15mg	Univasc	One	\$46	
Moexipril 15mg	Generic	One	\$30	
Perindopril 2mg	Aceon	One	\$48	
Perindopril 4mg	Aceon	One	\$56	
Perindopril 8mg	Aceon	One	\$68	
Quinapril 10mg	Accupril	One	\$46	
Quinapril 10mg	Generic	One	\$38	

**Table 4. ACEI Cost Comparison and Best Buy Indication**

Generic Name and Dose	Brand Name <sup>1</sup>	Frequency of Use (per day)	Average Monthly Cost <sup>2</sup>	Best Buy Indication
Quinapril 20mg	Accupril	One	\$46	
Quinapril 20mg	Generic	One	\$38	
Quinapril 40mg	Accupril	One	\$46	
Quinapril 40mg	Generic	One	\$38	
 Ramipril 1.25mg	Altace	One	\$44	Diabetes, Kidney Disease
 Ramipril 2.5mg	Altace	One	\$50	Diabetes, Kidney Disease
 Ramipril 5mg	Altace	One	\$54	Diabetes, Kidney Disease
 Ramipril 10mg	Altace	One	\$65	Diabetes, Kidney Disease
Trandolapril 1mg	Mavik	One	\$41	
Trandolapril 2mg	Mavik	One	\$42	
Trandolapril 4mg	Mavik	One	\$41	

1. "Generic" indicates that this drug is sold under its generic name. For example, in this table, the first drug listed is available as both generic benazepril and as brand-name Lotensin. Both have the same active ingredient. When column 2 says "generic," the price listed is for the generic version at the specified dose.
2. Prices reflect nationwide retail average for January 2005, rounded top the nearest dollar; data provided by NDCHealth, a health care information company.



## The Evidence

*This section presents more information on the effectiveness and safety of ACEIs.*

This report is based on an analysis of the scientific evidence on ACEIs. Slightly more than 6,000 studies were identified and screened. They were either published in the peer-reviewed medical literature (worldwide) or submitted by pharmaceutical companies. From these studies, the analysis focused on less than 150 meeting a set of criteria. Most of these were controlled clinical trials or “meta-analyses” of multiple clinical trials. A meta-analysis study combines the results of previous individual studies and tries to draw conclusions based on all of them.

### How Effective Are ACEIs?

ACEIs are highly effective medicines. A substantial body of evidence indicates that they improve quality of life and prevent both non-fatal and fatal heart attacks and strokes in a fairly wide range of patients with high blood pressure, heart disease, diabetes and kidney disease.

Unfortunately, no large-scale studies have been specifically designed to compare the ACEIs to each other in term of either effectiveness or safety. However, many studies evaluating various treatment regimens and combinations for high blood pressure, heart disease, and diabetes have included one or more ACEIs.

Overall, such studies have yielded mixed results for ACEIs compared to other medicines. Some show ACEIs to be superior and other studies have found no advantage for ACEIs. Notably, a study published in 2003 (known as the Second Australian National Blood Pressure Study) indicated that ACEIs were superior to diuretics in preventing heart attacks, strokes, and deaths among elderly men with high blood pressure. Another, more recent, study found that an ACEI (perindopril) combined with a drug called amlodipine (a calcium-channel blocker) was superior to a regimen of a beta-blocker and a diuretic in preventing heart attacks and strokes in people with high blood pressure. But several other well-done studies have found diuretics to be better in

people of all ages, either alone or combined with a beta-blocker, ACEI or calcium channel blocker.

A debate in the medical community over these divergent results has been underway – and quite contentious – for several years, and is likely to continue. Your doctor will probably be aware of that debate and he or she may have an opinion about the studies.

If you have significantly elevated blood pressure and one or more other heart conditions, this debate may be of more than passing interest to you. You should talk with your doctor about the best combination of drugs for you. *Using the right drugs at the right doses can be literally a life-and-death issue for you.* Unfortunately, it is not possible yet to say with certainty what the best combination of heart drugs is for many people who have several heart ailments.



Some of the strongest evidence for the benefit of ACEIs is from studies in people with heart failure, or of ACEI use to slow the progression of heart failure. Most studies show a clear case for the drug versus placebo. And about a dozen trials have compared one ACEI to another in the treatment of heart failure. The majority of these studies do not find a superiority of one ACEI over another. However, the evidence is stronger for some ACEIs than others, as addressed above in the *Best Buy* Picks section.

### How Safe Are ACEIs?

ACEIs are generally safe medicines, with widespread use for more than 20 years. They have not been shown to cause any serious long-term or irreversible negative consequences, even after many years of use.

As with most medicines, ACEIs can cause some annoying side effects. The most common of these is an irritating dry cough, which may be quite persistent. It usually occurs within a month of starting an ACEI. If it persists, talk to your doctor about switching to another ACEI or even another class of medicine.

Most of the other side effects occur less commonly. These include headache, dizziness, fatigue, nausea, swollen ankles, loss of taste, excessively low blood pressure, high blood levels of potassium, and renal failure.

Though rare, ACEIs can also cause swelling involving the face, tongue, lips and larynx. This is called angioedema and is a potentially life-threatening complication if it closes off the larynx. The risk of this side effect appears to be higher in African-Americans.

All ACEIs can also cause birth defects and should not be used by women who are pregnant.

There is no clear evidence that any one ACEI has more or fewer side effects than the others. The risk of all the ACEI-triggered side effects is greater for

people who take an ACEI along with another medication for high blood pressure, such as a diuretic. If side effects persist, talk to your doctor about adjusting your dose of the medicines.

People who take multiple medicines are more likely to discontinue taking them, too, due to side effects. *You should not stop taking your blood pressure medicines without consulting your doctor. That can be dangerous.*

All people taking ACEIs should have periodic blood tests to make sure they do not have elevated level of potassium in their blood and that their kidneys are processing the drug effectively. People who take lithium, nonsteroidal anti-inflammatory drugs, potassium or potassium-sparing diuretics (such as spironolactone, triamterene and epleronone) are at higher risk of developing these complications.

### Age, Race, and Gender Differences

As cited above, one study has indicated that one ACEI may be selectively effective in elderly people. But it is too premature to say whether all ACEIs are more effective or safer among older people than other blood pressure and heart medicines.

ACEIs may, however, be somewhat less effective in women than in men, studies indicate. But there is no evidence that any one ACEI has an advantage over any other among women.

ACEIs appear to be as effective in African-Americans as in other population groups. But African-Americans may need to take higher doses of ACEIs than whites, or use them in combination with a diuretic, to achieve a similar clinical benefit. Ramipril is one of the few drugs in any class proven to improve long-term outcomes in a trial conducted exclusively in African Americans. The trial showed that ramipril reduced the risk of end-stage renal disease and death in patients with kidney disease.

## Talking with Your Doctor

It's important for you to know that the information we present here is not meant to substitute for a doctor's judgment. But we hope it will help your doctor and you arrive at a decision about which ACEI and dose is best for you and which gives you the most value for your health-care dollar.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctor and that studies show doctors do not routinely take price into account when prescribing medicines. Unless you bring it up, your doctors may assume that cost is not a factor for you.

Many people (including physicians) believe that newer drugs are better. While that's a natural assumption to make, it's not true. Studies consistently show that many older medicines are as good as, and in some cases better than, newer medicines. Think of them as "tried and true," particularly when it comes to their safety record. Newer drugs have not yet met the test of time, and unexpected problems can and do crop up once they hit the market.

Of course, some newer prescription drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer versus older medicines, including generic drugs.

Prescription medicines go "generic" when a company's patents on a drug lapse, usually after about 12 to 15 years. At that point, other companies can make and sell the drug.

Generics are much less expensive than newer brand-name medicines, but they are not lesser quality drugs. Indeed, most generics remain useful medicines even many years after first being marketed. That is why today about 47% of all prescriptions in the U.S. are for generics.

Another important issue to talk with your doctor about is keeping a record of the drugs you are taking. There are several reasons for this:

- First, if you see several doctors, each may not be aware of medicines the others have prescribed.
- Second, since people differ in their response to medications, it is very common for doctors today to prescribe several medicines before finding one that works well or best.
- Third, many people take several prescription medications, nonprescription drugs and dietary supplements at the same time. These can interact in ways that can either reduce the benefit you get from the drug, or be dangerous.
- And fourth, the names of prescription drugs — both generic and brand — are often hard to pronounce and remember.

For all these reasons, it's important to keep a written list of all the drugs and supplements you are taking and to periodically review this list with your doctors.

Always be sure, too, that you understand the dose of the medicine being prescribed for you and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at the pharmacy or if you get it by mail, you may want to check to see that the dose and the number of pills per day on the pill bottle match the amounts that your doctor told you.

## How We Picked the *Best Buy* ACEIs

Our evaluation is based on an independent scientific review of the evidence on the effectiveness, safety and adverse effects of ACEIs. A team of physicians and researchers at the Oregon Health & Science University Evidence-based Practice Center conducted the analysis as part of the Drug Effectiveness Review Project, or DERP. DERP is a first-of-its-kind 12-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of the ACEIs forms the basis for this report. A consultant to *Consumer Reports Best Buy Drugs* is also a member of the Oregon-based research team, which has no financial interest in any pharmaceutical company or product.

The full DERP review of ACEIs is available at <http://www.ohsu.edu/drugeffectiveness/reports/final.cfm> (Warning: this is a long and technical document written for physicians and experts.)

The drug costs we site were obtained from a health-care information company that tracks the sales of prescription drugs in the United States. Prices for a

drug can vary quite widely, even within a single city or town. All the prices in this report are national averages based on sales of prescription drugs in retail outlets. They reflect the cash price paid for a month's supply of each drug in January 2005.

Consumers Union and *Consumer Reports* selected the *Best Buy Drugs* using the following criteria. The drug (and dose) had to:

- Be in the top tier of effectiveness among the 10 ACEIs.
- Have a safety and side effect record equal to or better than other ACEIs.
- Have an average price for a 30-day supply that is substantially lower than the most costly ACEIs meeting the first two criteria

The *Consumers Reports Best Buy Drugs* methodology is described in more detail in the methods section at [www.CRBESTBUYDRUGS.ORG](http://www.CRBESTBUYDRUGS.ORG).

## About Us

Consumers Union, publisher of *Consumer Reports* magazine, is an independent and nonprofit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and to create a fair marketplace. Its Web site is [www.consumersunion.org](http://www.consumersunion.org). The magazine's Web site is [www.consumerreports.org](http://www.consumerreports.org).

*Consumer Reports Best Buy Drugs* is a public education project administered by Consumers Union. Two outside sources of generous funding made the project possible. They are a major grant from the Engelberg Foundation, a private philanthropy, and a supporting grant from the National Library of Medicine, part of the National Institutes of Health. A more detailed explanation of the project is available at [www.CRBESTBUYDRUGS.ORG](http://www.CRBESTBUYDRUGS.ORG).

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Best Buy Drugs* Web site is accurate and describes generally accepted clinical practices. If we find, or are alerted to, an error, we will correct this as quickly as possible. However, *Consumer Reports* and its authors, editors, publishers, licensors and any suppliers cannot be responsible for medical errors or omissions, or any consequences from the use of the information on this site. Please refer to our user agreement at [www.CRBESTBUYDRUGS.ORG](http://www.CRBESTBUYDRUGS.ORG) for further information.

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