

Consumer Reports BEST BUY DRUGS™

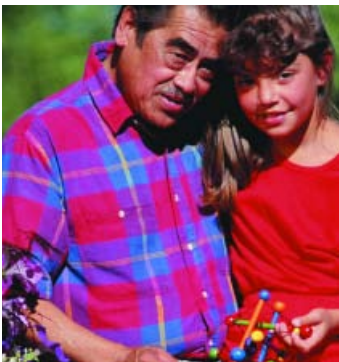
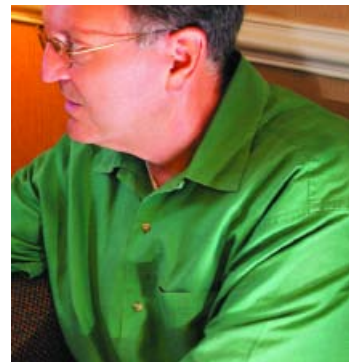
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Treating Elevated Cholesterol and Heart Disease:

The Statins

Comparing Effectiveness, Safety, and Price



Our Recommendations

The cholesterol-lowering medicines known as “statins” are highly effective and generally safe. In people at risk for heart disease or who have heart disease, statins substantially lower the chances of a heart attack and death.

There are six statins and they differ in their ability to reduce cholesterol. In addition, the evidence is stronger for some statins when it comes to reducing your risk of heart attack or death from heart disease or stroke. Thus, the choice of the best statin for you can be complex.

The statins vary widely in cost as well – from about \$32 a month to more than \$150 a month. Most people who take statins must take the medicine for years, so the cost matters.

Taking the evidence for effectiveness, safety, and cost into account, we have chosen four statins as *Consumer Reports Best Buy Drugs*, under different circumstances:

- *Generic lovastatin or pravastatin* – if you need to lower “bad” (LDL) cholesterol by less than 30%
- *Generic simvastatin (20mg or 40 mg)* – if you need 30% or greater LDL reduction and/or have heart disease or diabetes, or if you have had a heart attack or have acute coronary syndrome and your LDL level is not highly elevated.
- *Atorvastatin (Lipitor) (40mg or 80mg)* – if you have had a heart attack or have acute coronary syndrome and your LDL is highly elevated; use for two years and then reconfirm need or switch to generic simvastatin.

Generic pravastatin and simvastatin became available in 2006. The price of these two medicines will decline in 2007, creating a significant savings opportunity compared to brand-name statins.

Most people who need a statin should take the lowest dose that reduces their LDL cholesterol to an acceptable “target” level. High doses of statins pose greater risk – of muscle and liver problems. But some people – such as those who have had a heart attack – may need a higher dose.

No matter what dose you take, if you experience muscle aches and pains when taking a statin, contact your doctor immediately. Also ask your doctor about splitting your statin pills. This can save you money and is a widely accepted practice.

This report was last updated in February 2007.

Welcome

The statins are among the most widely prescribed medicines in the world. They are used to treat high cholesterol and heart disease. Their use has increased sharply in recent years. Between 10% and 15% of people aged 20 and older in the U.S. now take a statin, and one in four people age 65 and older do.

This report updates one done in June 2006. It discusses new recent research on the statins, and includes updated prices (as of December 2006). It also includes an updated discussion of the savings available through two new generic statins that went on the market in the second half of 2006 – pravastatin and simvastatin. The brand-name versions of these two drugs – Pravachol and Zocor, respectively – had been widely prescribed for many years. The generics now take their place.

This report compares the statin drugs to each other and will help you talk with your doctor about your statin choices and heart disease risk. It 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, other drugs we have evaluated, and to get cost updates, visit www.CRBestBuyDrugs.org.

Statins' effectiveness in reducing the risk of heart attack and stroke has underscored the importance of cholesterol screening. The National Institutes of Health and the National Cholesterol Education Program advises *all people 20 years and older* to get their cholesterol checked at least *once every five years*. If you are at risk for heart disease for other reasons (smoking, diabetes, or high blood pressure, for example), you should get it checked more often.

Your cholesterol test should include measures of your LDL and HDL levels. LDL stands for “low density lipoprotein” and is the “bad” cholesterol. HDL stands for “high density lipoprotein;” it’s the “good” cholesterol. Today, those measures are more meaningful than your total cholesterol, which generally should be below 200mg/dl (milligrams per deciliter of blood). (See Table 1 on page 5) Your doctor is also likely to measure your triglyceride levels. This is a type of fat that has been linked to heart disease; statins also lower triglycerides. He or she may also want to check your blood levels of a substance called C-reactive protein, which is a marker for artery inflammation.

The increase in statin prescriptions has also spurred controversy. Some doctors and public health advocates are concerned that too many people are turning to statin drugs before trying to lower LDL cholesterol through dietary and lifestyle change. Studies show that LDL cholesterol can be lowered – generally by 7% to 12% -- by even modest reductions of saturated fat in the diet. And diets rich in vegetables and fruits have been associated with lower overall risk of premature heart disease. Studies also show that regular aerobic exercise helps raise HDL levels.

There is general medical consensus that all people who need to lower their LDL levels should modify their diets *whether or not they are prescribed a statin*. But there is no medical consensus on who needs to lower cholesterol initially by diet alone and who should start taking a statin as initial therapy for elevated LDL cholesterol.

With an estimated 70 to 80 million Americans having elevated LDL levels, but only around 20 million taking statins, the question is an important one. Should millions more people be taking these medicines, or should most of them be trying to reduce cholesterol through diet and exercise first?

There's no easy answer to this question, and we leave the decision to your doctor and you as it is beyond the scope of this report to compare diet versus drugs in the treatment of elevated cholesterol. We would reiterate, however, that knowing your cholesterol levels will help inform this decision. People with very high LDL levels are unlikely to be able to lower them enough through diet or exercise alone.

Six statins are now available by prescription in the U.S. One other drug combines a statin with another type of cholesterol-lowering drug. The seven drugs are:

Generic Name	Brand Name(s)	Available as a Prescription Generic Drug?
Atorvastatin	Lipitor	No
Fluvastatin	Lescol, Lescol XL	No
Lovastatin	Mevacor, Altoprev	Yes
Pravastatin	Pravachol	Yes
Simvastatin	Zocor	Yes
Simvastatin/Ezetimibe	Vytorin	No
Rosuvastatin	Crestor	No



Other cholesterol-lowering medicines are available, but they are less widely prescribed. Talk to your doctor about whether these other medicines – such as niacin (Niacor) or ezetimibe (Zetia) – may be useful for you, possibly in combination with a statin.

And, again, talk with your doctor or a nutritionist about dietary changes that could help lower your cholesterol. Even after years of attention to this issue, many people remain confused about what constitutes a cholesterol-lowering and heart-healthy diet. For example, many Americans still believe that cutting eggs out of their diet will do the trick. It won't if the rest of your diet is high in saturated fats from meat, margarine, butter, and other high-fat dairy products.

This report was last updated in February 2007.

What Are Statins and Who Needs Them?

Statins work by blocking an enzyme needed to make cholesterol. The body needs cholesterol to maintain good health. But high blood levels of LDL cholesterol and low levels of HDL cholesterol are very clearly associated with an increased risk of arterial blockage throughout the body that can eventually lead to heart attack and stroke, and peripheral artery disease in the legs. Statins may also help lower the risk of heart attack and stroke by reducing inflammation in arteries.

Your doctor may prescribe a statin if blood tests determine that you have high LDL cholesterol (above 160 mg/dl for some; 130 mg/dl for others) or low HDL cholesterol (below 40mg/dl for most people), and if diet and exercise changes fail or are unlikely to bring your LDL level down to an acceptable level.

Your doctor also may prescribe a statin, irrespective of your LDL or HDL levels, if you:

- Have other conditions or habits, such as diabetes, high blood pressure or cigarette smoking that already put you at high risk of having a heart attack or stroke.
- Have known coronary artery or cerebrovascular disease
- Have already had a heart attack or stroke
- Have acute coronary syndrome (ACS), a diagnosis that encompasses anyone with chest pain and EKG (electrocardiogram – a test) signs of coronary artery disease.

Your doctor will likely recommend a healthy "target" LDL level, which will depend on your medical history and your overall risk of heart disease and stroke.

For most people who are prescribed a statin, the target will be to lower their LDL cholesterol to 130mg/dl or less. However, new recommendations from the National Institutes of Health and the American Heart Association indicate that an LDL level of 100mg/dl or lower may be desirable for many people and an LDL level of 70mg/dl or even lower may be desirable for those at highest risk of heart attack or stroke. Tables 1 and 2 on this page and the next page give a quick rundown of this latest advice on cholesterol lowering.

Table 1. What Should Your Cholesterol Levels Be?*	
Total Cholesterol Level	Category
Less than 200mg/dl	Desirable
200-239mg/dl	Borderline
240mg/dl and above	High
LDL Cholesterol Level	Category
Less than 100mg/dl	Optimal
100-129mg/dl	Okay but less than optimal
130-159mg/dl	Borderline high
160-189mg/dl	High
190mg/dl and above	Very High
HDL Cholesterol Level	Category
Less than 40mg/dl	Risky, not good
41-59mg/dl	Okay but less than optimal
60mg/dl and above	Good, helps lower risk

* This table applies primarily to people with no other risk factors for heart disease
 Source: Adapted from National Cholesterol Education Program, *High Blood Cholesterol – What You Need to Know*, Revised June 2005. NIH Publication No. 05-3290

Once your doctor advises use of a statin, you both face a decision about which one and at what dose. This decision has become more important in recent years as evidence has mounted that (a) the statins differ in their potency and (b) the effectiveness *and potential harmful effects* of statins is increased with the use of larger doses. For some people, however, aggressively lowering LDL cholesterol may be needed to more substantially lower their risk of heart attack and stroke. This may involve a stricter diet with a lower dose of statin or it could involve taking a more potent statin or a higher dose of a statin. The next section discusses your choices.



Table 2. Latest Advice on LDL Cholesterol Reduction¹

Risk Group	Criteria and Factors ²	LDL should be: ³
Low Less than 10% chance of heart attack or death from heart disease over 10 years	-No current heart disease -No or only one risk factor	-Below 160mg/dl -Below 130mg/dl is better
Moderate 10% chance of heart attack or death from heart disease over 10 years	-No current heart disease -Two risk factors	-Below 130mg/dl -Below 100mg/dl is better
Moderately High 10% to 20% chance of heart attack or death from heart disease over 10 years	-Two or more risk factors	-Below 130mg/dl -Below 100mg/dl is better
High Greater than 20% chance of heart attack or death from heart disease over 10 years	-Known heart or blood vessel disease -Diabetes -Multiple risk factors	-Below 100mg/dl -Below 70mg/dl is better

(1) Adapted from the National Cholesterol Education Program, National Institutes of Health, July 2004; *Circulation* (July 13, 2004): Vol.110, pages 227-239

(2) In addition to having an elevated LDL and/or low HDL, the most important risk factors for heart disease, heart attack, and stroke are cigarette smoking, having diabetes and/or high blood pressure. Other risk factors include being overweight, getting no or very little exercise, having elevated triglyceride levels, and having a family history of early heart disease.

(3) mg/dl stands for milligrams per deciliter of blood. Your doctor can explain this measure.



Choosing a Statin – Our *Best Buy* Picks

All the statins have been shown to reduce blood levels of LDL cholesterol. And most have been shown to lower the risk of heart attack and death from heart disease.

But the statins differ in their ability to reduce LDL cholesterol. And the evidence is stronger for certain statins when it comes to reducing your risk of heart attack or death from heart disease or stroke.

The statins also vary widely in cost. As mentioned, three are now available as generics, and you can save a significant amount of money if you and your doctor choose one of the generics. This may also help you stay on the drug. If you have no insurance or have Medicare's new Part D drug coverage, choosing a generic statin is especially likely to make your drug bill more affordable.

Tables 3 and 4 on pages 8 and 10 present the average retail prices for all statins, reflecting the price at stores nationwide. These prices are as of December 2006. As you can see, as of that month:

- Lovastatin costs an average \$32 to \$58 a month, depending on dose
- Pravastatin costs from \$68 to \$143 a month, depending on dose
- Simvastatin costs from \$63 to \$140 a month, depending on dose

In the first half of 2007, the price of the new generics – pravastatin and simvastatin – should decline significantly. That's because other generic drug companies will now be able to make the drugs and compete in the marketplace. By some predictions, pravastatin's price could fall to between \$15 and \$30, and simvastatin's to between \$25 and \$40.

Be sure to check prices at online pharmacies and large discounts stores, too. You may want to purchase there, or just compare prices. We checked prices for the two new generics at prominent online pharmacies in late January 2007, for example, and found simvastatin 10mg available for as low as \$51 for a month's supply. The 20mg dose was selling for between \$89 and \$130 for a month's supply. In both cases, the lowest price was available only with a purchase of a 90-day supply. (Prices do not include shipping.)

Even bigger savings could be achieved for pravastatin. At one online pharmacy, a month's supply of the 20mg dose was selling for just \$18. At another, it was \$27. These online prices signal the declining prices for these drugs. Pravastatin is also one of Wal-Mart's and Target's generic \$4 drugs, for a 30-day supply. It may be hard to beat that price.

Of course, price is not the only important factor in choosing a statin. You and your doctor will want to consider:

- The amount of LDL cholesterol reduction required to meet your target LDL level
- Your risk factors for heart disease
- The strength of evidence for each statin
- The possibility of drug interactions with medicines you are already taking

Our recommendations are for three groups of people who need statins:







- (1) Those who require LDL reductions of less than 30% to reach their target LDL
- (2) Those who require LDL reductions of 30% or more, and/or have heart disease or diabetes
- (3) Those who have had a heart attack or have acute coronary syndrome (ACS)

The 30% differentiation point is not arbitrary. Most people with elevated cholesterol have only slightly or moderately elevated LDL levels, and may simply not need one of the more potent statins. Another reason the 30% differentiation point makes sense is that the statin drugs fall along a spectrum in their potency. All of the more potent drugs are capable of yielding a 30% or greater LDL reduction for most people while the less potent statins are generally less effective in bringing about a 30% or greater decline in LDL. Tables 3 and 4 give you a run down of average statin potency. Remember, your actual LDL reduction may vary from the averages or ranges given in these tables.

If you require LDL reduction of less than 30%

To orient you, this would mean that if you have an LDL of 170 mg/dl, and you had no heart disease risk factors, your doctor may want to get that down to at least 130 mg/dl. That would be a decline of 24%.

Table 3. Statin Choices for People Who Require LDL Lowering of Less than 30%

Generic Name And Dose Per Day	Brand Name ¹	Average Monthly Cost ²	Average Expected LDL Reduction	Reduces the Risk of Heart Attack? ³	Mortality Reduction?
Atorvastatin				Yes	Yes
Atorvastatin 10mg	Lipitor	\$93	34%-38%		
Atorvastatin 20mg	Lipitor	\$133	42%-46%		
Ezetimibe/simvastatin				Yes ⁴	Yes ⁴
Ezetimibe/simvastatin 10mg/10mg	Vytorin	\$112	45%		
Ezetimibe/simvastatin 10mg/20mg	Vytorin	\$111	52%		
Fluvastatin				Likely	Likely
Fluvastatin 20mg	Lescol	\$79	22%		
Fluvastatin 40mg	Lescol	\$78	25%		
Lovastatin				Yes	Likely ⁵
 Lovastatin 10mg	Generic	\$32	21%		
 Lovastatin 20mg	Generic	\$37	24%-27%		
 Lovastatin 40mg	Generic	\$58	31%		
Lovastatin 20mg longacting	Altoprev	\$108	30%	Yes ⁶	Likely ⁶
Lovastatin 40mg longacting	Altoprev	\$116	36%		
Pravastatin				Yes	Yes
Pravastatin 10mg	Pravachol	\$120	18%-25%		
Pravastatin 20mg	Pravachol	\$114	23%-29%		
Pravastatin 40mg	Pravachol	\$168	26%-34%		
 Pravastatin 10mg	Generic	\$70 ⁷	18%-25%		
 Pravastatin 20mg	Generic	\$68 ⁷	23%-29%		
 Pravastatin 40mg	Generic	\$90 ⁷	26%-34%		
Rosuvastatin				Likely	Likely
Rosuvastatin 5mg	Crestor	\$112	39%-46%		
Simvastatin				Yes	Yes
Simvastatin 10mg	Zocor	\$98	26%-33%		
Simvastatin 20mg	Zocor	\$169	30%- 40%		
Simvastatin 10mg	Generic	\$83	26%-33%		
Simvastatin 20mg	Generic	\$140	30%- 40%		

(1) "Generic" indicates drug sold by generic name.

(2) Prices reflect nationwide retail average for December 2006, rounded to nearest dollar; information derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite.

(3) Nonfatal and fatal heart attack plus deaths attributed to heart disease.

(4) The combination of these two drugs has not been proven but simvastatin has. The benefit is assumed for the combination.

(5) Lovastatin has not been proven to reduce deaths, but the evidence strongly points in that direction.

(6) Based on the results for shorter-acting versions of the drugs.

(7) Price will decline in 2007, by half if not more, due to generic competition.

Taking the evidence for effectiveness, safety, and cost into account, generic lovastatin and pravastatin are our *Best Buy* choices for people in this category. They have about the same potency, as you can see from Table 3. The average LDL reduction you can expect with generic lovastatin is 21% to 31%, depending on dose. With pravastatin, it's 18% to 34%.

As mentioned, within a few months, both these medicines will likely be around the same price.

Generic simvastatin is also an option for some people in this category. If your LDL hovers close to 30% above where it should be, your doctor may advise this more potent statin, especially if you have a family history of heart disease and/or are overweight and sedentary.

No matter how elevated your LDL, if it doesn't decline as much as needed after a month or so of taking lovastatin or pravastatin, your doctor could choose to prescribe simvastatin, another statin, or a second cholesterol-lowering drug to be taken along with a statin. Options for a second drug are ezetimibe (Zetia), generic niacin, or colesvelam (Welchol). The added cost may be a consideration, however, and especially with ezetimibe and colesvelam. Neither are available as generics. Taking lovastatin plus generic niacin, which generally costs less than \$15 for a month's supply, may be best. Niacin has the added benefit of increasing HDL levels. But it may also slightly increase the risk of muscle problems. Note that there's less proof these non-statins reduce heart attacks and strokes.

If you are now taking one of the other more expensive brand-name statins and your LDL was in fact only marginally elevated when you began taking it, we suggest talking with your doctor. It may be that your health insurance or pharmacy benefit plan preferentially covers that statin. If so, you may want to stick with it if your co-pay for the drug is the lowest available under your insurance plan. Be aware, though, that in many health insurance plans now, all generics have a lower co-pay (usually \$5-\$10) than brands (\$25 or more). So if you are taking a brand-name statin (Lipitor, Crestor or Vytorin) and paying \$25 each time you fill a prescription, you will save money by switching to generic lovastatin or pravastatin if your doctor agrees this is an option for you.

If you require LDL reduction of 30% or more, and/or have heart disease or diabetes

For example, if your total cholesterol is 220 mg/dl, your LDL is 175 mg/dl, and you have diabetes and other risk factors for heart disease, your doctor may set a target LDL for you of 100 mg/dl. That's a 43% decline in your LDL and will require you to take a more potent statin.

Table 4 on the next page presents your statin options if you are in this category. Taking the evidence for effectiveness, safety, and cost into account, we have chosen generic simvastatin (20mg, 40mg) as the *Best Buy* drug.

Simvastatin is a proven medicine with a long track record. The 20mg and 40mg doses reduce LDL by 30% to 45%, and have been shown to reduce heart attacks and death from heart disease. The drug is on most if not all insurance company, health plan (HMO, PPO) and government (Medicare Part D) drug formularies.

As mentioned, the cost for this medicine should be declining in the months ahead. If you are still taking Zocor, the brand-name version of simvastatin, talk to our doctor as soon as possible about switching to the generic.

If you are taking any other statin, we advise talking with your doctor about whether you should stay on it or switch to simvastatin. For most people, switching may be a good idea. But for some it will not be. In particular, if you are one of the 10% of people with high cholesterol whose LDL is very high (50% or more than it should be), your doctor may advise staying on the statin you are on – for example, Lipitor, Crestor, or Vytorin. This may be a better strategy than taking the highest (80mg) dose of simvastatin, which some studies indicate carries a higher risk of muscle problems.

In addition, if you are now taking 40mg or 80mg of Lipitor or 20mg or 40mg of Crestor and you switch to 40mg of simvastatin, your LDL could rise. The increase may be minor. Your personal medical and financial circumstances should determine your choice in this case.

Remember, though, that a switch to simvastatin could save you thousands of dollars over the many years you may have to take a statin. For example, even if the price of Lipitor comes down to, say, \$80 a month

and has a co-pay of \$25, generic simvastatin could cost only \$25 to \$40 a month with perhaps a \$7 co-pay. For people with insurance, that \$18 difference (between \$7 and \$25 out of pocket) translates into

potential a savings of \$216 per year, or \$3,240 over 15 years. (And don't forget the even larger savings for your employer or insurer, which helps keeps a lid on rising health insurance premiums.)

Table 4. Statin Choices for Higher Risk People

Generic Name With Dose Per Day	Brand Name ¹	Average Monthly Cost ²	Average Expected LDL Reduction	Reduces the Risk of Heart Attack? ³	Mortality Reduction?
Atorvastatin				Yes	Yes
Atorvastatin 20mg	Lipitor	\$133	42% to 46%		
CR BEST BUY Atorvastatin 40mg	Lipitor	\$133	47% to 51%		
CR BEST BUY Atorvastatin 80mg	Lipitor	\$133	46% to 54%		
Ezetimibe/simvastatin				Yes ⁴	Yes ⁴
Ezetimibe/simvastatin 10mg/10mg	Vytorin	\$112	45%		
Ezetimibe/simvastatin 10mg/20mg	Vytorin	\$111	52%		
Ezetimibe/simvastatin 10mg/40mg	Vytorin	\$111	55%		
Ezetimibe/simvastatin 10mg/80mg	Vytorin	\$110	60%		
Fluvastatin				Likely	Likely
Fluvastatin XL 80mg	Lescol XL	\$101	35%		
Lovastatin				Yes	Likely ⁶
Lovastatin 80mg ⁵	Generic	\$116	39%-48%		
Lovastatin 60mg long-acting	Altoprev	\$121	40%		
Pravastatin				Yes	Yes
Pravastatin 80mg	Pravachol	\$173	30%-37%		
Pravastatin 80mg	Generic	NA ⁷			
Rosuvastatin				Likely	Likely
Rosuvastatin 10mg	Crestor	\$109	43%-50%		
Rosuvastatin 20mg	Crestor	\$108	52%-55%		
Rosuvastatin 40mg	Crestor	\$106	55%-60%		
Simvastatin				Yes	Yes
Simvastatin 20mg	Zocor	\$187	30%-40%		
Simvastatin 40mg	Zocor	\$184	35%-45%		
Simvastatin 80mg	Zocor	\$177	40%-50%		
CR BEST BUY Simvastatin 20mg	Generic	\$140 ⁸	30%-40%		
CR BEST BUY Simvastatin 40mg	Generic	\$140 ⁸	35%-45%		
Simvastatin 80mg	Generic	\$136 ⁸	40%-50%		

(1) "Generic" indicates drug sold by generic name.

(2) Prices reflect nationwide retail average for December 2006, rounded to nearest dollar; information derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite.

(3) Nonfatal and fatal heart attack plus deaths attributed to heart disease.

(4) The combination of these two drugs has not been proven but simvastatin has. The benefit is assumed for the combination

(5) Requires taking two 40 mg tablets.

(6) Lovastatin has not been proven to reduce deaths, but the evidence strongly points in that direction.

(7) Just approved in November 2006. Price not yet available.

(8) Price will decline sharply in 2007 due to generic competition.

For people who have no health insurance or drug coverage, the savings are of course much larger.

If you have had a heart attack or have acute coronary syndrome

Heart attack victims are at very high risk of another (possibly fatal) heart attack and generally benefit from lowering their LDL cholesterol as much as possible. The same goes for people with acute coronary syndrome, or ACS.

Heart attack victims and people with ACS will generally be prescribed several different kinds of drugs, including a statin. In addition, lifestyle changes will be strongly urged. If their LDL is not highly elevated, a doctor may choose to prescribe simvastatin 40mg. One notable recent study yielded favorable results for simvastatin 40mg in preventing second heart attacks and deaths; it was compared to 80mg of Lipitor.

However, heart patients taking Lipitor fared well in that study, too (as they have in other studies), especially when it came to counting the reduction in strokes and the need for heart surgery. In addition, Lipitor may be a better option for people who have had a heart attack or have ACS and need greater LDL reduction. It has a superior safety track record at the maximum potency dose of 80mg, too, which may be needed for this group.

Thus, for people in this category, we choose both generic simvastatin and Lipitor as *Best Buys*. Lipitor

is not available as a generic and is thus more expensive. Our choice of Lipitor comes with a caveat. For cost reasons and until further evidence emerges, we advise Lipitor use for two years only if it is prescribed just after a heart attack or diagnosis of ACS.

After that, if you have not had another heart attack in that period and your LDL has been reduced to target, you and your doctor should consider switching to simvastatin 40mg. This switch presumes lifestyle changes that will have lowered your heart attack risk.

Vytorin and the other statins

The newest statin, Vytorin, contains simvastatin in combination with ezetimibe. Ezetimibe works differently than a statin. It reduces LDL cholesterol by absorbing dietary cholesterol. Vytorin is a potent LDL reducer, and has been much advertised to consumers. These ads have played up the combination – sending a message that your blood cholesterol comes from two sources, your heredity (genetics) and the food you eat.

This drug may prove useful for some people, but we advise taking these ads with a grain of salt since there is no evidence that Vytorin works better than other potent statins, including generic simvastatin, in preventing heart attacks or strokes. We will be closely following the evidence on Vytorin in the months ahead.

What about the other statins? As you can see in Table 4, fluvastatin XL (Lescol XL) and rosuvastatin (Crestor)

Table 5. Statin Choices for People With Special Considerations

Consideration	Frequently Recommended Statins ¹	Comment
Kidney transplant patients taking cyclosporine	Fluvastatin (Lescol) Pravastatin (Pravachol)	Both are safe and effective. Lescol is less proven than Pravastatin.
HIV positive patients taking protease inhibitors ²	Atorvastatin (Lipitor) Fluvastatin (Lescol) Pravastatin (Pravachol)	Low doses are strongly advised.
Patients taking gemfibrozil (Lopid)	Atorvastatin (Lipitor) Lovastatin (generic) Simvastatin (Zocor)	Follow FDA warnings.
Patients taking warfarin (Coumadin)	All statins	May require adjustment in dose of the blood thinner.

(1) Because they have been shown effective in this population of patients

(2) Protease inhibitors are indinivir, nelfinavir, ritonavir, saquinavir, amprenavir, lopinavir/ritonavir.

are priced in the same range as Vytorin. Lescol delivers less LDL lowering and although Crestor delivers a higher range of LDL lowering, both drugs have not been shown to reduce heart attacks and deaths as have the other statins. Additionally, Crestor may have safety issues, although it is not yet certain if the risks are different from other statins.

Warning about high doses

There is one other important issue you should know about as you and your doctor choose a statin. For people who are at high risk of heart attack – for example, if you have diabetes, are a smoker and have elevated LDL levels – recent studies indicate that the lower your LDL, the lower the risk of heart attack and stroke. Since higher doses of statins reduce LDL cholesterol more than lower doses, the hypothesis has been that higher doses are better and should be used more liberally.

But other recent research has confused this picture. In one notable study, high doses of Lipitor (80mg) did not yield a lower incidence of “major coronary events” or death when compared to a medium dose (40mg) of simvastatin.

In addition, higher doses come with more risks. Higher doses of all statins have been linked to muscle aches, soreness, tenderness, or weakness. Up to one in 20 people who take a statin experience these symptoms, and up to 10% in some studies have not been able to tolerate an 80mg dose. Higher doses have also been linked to an increased risk of a life-threatening form of muscle breakdown called rhabdomyolysis. This can lead to permanent kidney damage and coma.

We advise caution with statin dosing. In general, you should take the lowest dose of a statin necessary to meet your LDL target, even if you need to lower your LDL by 30% or more. People who have been diagnosed with heart disease and especially those who have had a heart attack, may be advised to start with a higher dose (40mg or 80mg) and carefully monitor their side effects.

A word about strokes

Statins are widely prescribed for people who have had a stroke or “mini-stroke,” which doctors call a transient ischemic attack, or TIA. But the evidence

on statin treatment for people who have had strokes or TIAs has never been as strong as for people with heart disease and who have had a heart attack.

The latest study to look at this issue, published in August 2006, yielded mixed results that will prolong the controversy.

The study found that people who had a stroke or TIA and took a statin (the drug used in the study was Lipitor) had a decreased risk over five years of a subsequent stroke or TIA. But the decline in risk was quite small: 11.2% of the patients that took Lipitor had another stroke or TIA versus 13.1% of patients who took a placebo.

In addition, the patients who took Lipitor were substantially more likely to have the kind of stroke that involves bleeding in the brain, also called a hemorrhagic stroke. This kind of stroke is rarer than so-called ischemic strokes, which are caused by blood clots. But hemorrhagic strokes are much more likely to be severe, lead to greater long-term disability, and to death.

Notably, the patients in the study took 80mg of Lipitor, the highest dose. This led to speculation that the high dose may have increased the risk of hemorrhagic stroke. But that conclusion is uncertain. If you or a loved one is a stroke victim taking any statin, consult with your doctor about the results of this recent study.

People with special considerations

Table 5 on page 11 presents statin recommendations for people with certain medical conditions. Your doctor should help you determine which statin is safest and most effective if you have one of these conditions.

In particular, medicines for HIV and AIDS and those used to prevent rejection of transplanted organs can increase the toxicity of statins. Statins can also increase the effect of blood thinners, such as warfarin, and interact with many other medications, including those used to control blood pressure.

This is not a comprehensive list. Your doctor may advise a particular statin if you have other conditions or chronic diseases. It's wise to tell your doctor about any medicine you are taking, prescription or nonprescription.

Splitting Your Statin Pills

There is another way you can save money if you have to take a statin – split your pills. As you can see from Tables 3 and 4, some statins cost more at higher doses but others cost the same. Generic lovastatin varies in price, for example, for the 10mg, 20mg, and 40mg doses but Lipitor at doses of 20mg, 40mg, and 80mg cost the same. When larger doses cost the same as the smaller dose, you can save money by getting the larger dose and splitting the pills in half.

Several recent studies indicate that most statins can be split in half without any loss of effectiveness. Both government and private sector health facilities (including the Veteran’s Affairs health system) accept – and in some cases even encourage – this practice.

You should, however, consult your doctor before splitting your statin pills. Some people find pill splitting difficult to do.

If you and your doctor agree that you can split your pills, you will want to use a pill splitter to make certain that the two halves are the same size and therefore provide the correct dose each day. The simple devices cost \$5 to \$20 and are widely available. A good practice is to split your pills one at a time and take the second half as your next dose. For a guide to pill splitting, go to www.CRBESTBUYDRUGS.org.

Table 6. Pill Splitting Could Save You Money¹

Statin and Daily Dose	Average Monthly Cost ²	Monthly Savings if Larger Dose Split in Half	Resulting Average Monthly Cost with Split Pills
Lovastatin (generic) 10mg	\$32	\$13.50	\$18.50
Ezetimibe/simvastatin (Vytorin) 10mg/20mg	\$111	\$55.50	\$55.50
Atorvastatin (Lipitor) 10mg	\$93	\$26.50	\$66.50
Atorvastatin (Lipitor) 40mg	\$133	\$66.50	\$66.50
Pravastatin (generic) 10mg	\$70	\$36	\$34
Simvastatin (generic) 20mg	\$140	\$70	\$70

(1) In 3rd column – monthly savings – larger dose used for calculation is dose one size up from dose indicated in first column.

(2) Prices reflect nationwide retail average for December 2006, rounded to nearest dollar.

The Evidence

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

How Effective Are Statins?

Statins reduce the risk of a first heart attack and repeat heart attacks, as well as the risk of death from heart attacks, other forms of heart disease and overall. But some statins have been studied more extensively than others in terms of both their effectiveness and their safety. And ongoing research continues to define how the statins work and how they differ.

Generally, three criteria are used to measure the effectiveness of statins:

- Reduction of non-fatal heart attacks
- Reduction of deaths from heart attacks
- Reduction of death from other causes, including stroke and other forms of heart disease

Reduction of Heart Attacks

Four statins – atorvastatin (Lipitor), lovastatin, pravastatin, and simvastatin – have been proven to reduce the risk of heart attack over three to five years of use. And strong evidence indicates that their benefit outweighs any risk of harm due to side effects or problems associated with long-term use.

The evidence is less definitive for two other statins: fluvastatin (Lescol and Lescol XL) and rosuvastatin (Crestor). Rosuvastatin (Crestor), the newest statin, is currently being evaluated in long-term studies. Studies of Vytorin have not yet evaluated its effectiveness in reducing heart attacks. Approval of the drug by the FDA was granted on the basis that it's two active components – ezetimibe and simvastatin – have been separately evaluated. Simvastatin has been shown to reduce heart attacks in clinical trials. But ezetimibe has not.

Importantly, the statin drugs do not eliminate the risk of having a first or a repeat heart attack. In one three-year study assessing prevention of a first heart attack, 5% of people taking a placebo had a heart attack versus 3% taking a statin. And another recent study found that while people who did not have cardiovas-

cular disease, but did have one or more risk factors (and/or diabetes), benefited from taking a statin, the reduction in risk was not dramatic. Of those taking statins, 6.3% had a heart attack, coronary event, or stroke versus 8.1% of those taking a placebo.

Reduction of Deaths

The same four statins cited above have been shown to reduce deaths from heart attack in patients who have a history of heart disease, or risk factors for heart disease, such as diabetes and high blood pressure.

In addition, two of the statins – pravastatin and simvastatin – have been shown to reduce the overall risk of dying in people considered to be at low risk of heart disease or heart attack. A major study of lovastatin has strongly suggested a similar benefit. Lipitor has only been tested, and shown effective, in reducing deaths in high-risk patients. But here, too, the evidence strongly suggests that it would be effective in reducing deaths among low-risk people as well.

People Who Have Had a Heart Attack

Starting a statin at the time of a heart attack or very soon after can reduce the risk of death substantially – and this treatment is fast becoming a routine practice. In one important head-to-head study in people who had a heart attack, a high dose of atorvastatin (Lipitor, 80mg) proved to be more effective in reducing the death rate than a moderate dose of pravastatin (40mg). In a second recent study, 80mg of Lipitor reduced non-fatal heart attacks more than a 20mg dose of simvastatin but, importantly, there was no significant difference in the number of deaths among people who took the two different drugs and doses.

How Safe Are Statins?

Overall, the statins appear to be quite safe. But they can have two important adverse effects: muscle tissue damage and liver damage. Women who are pregnant or trying to become pregnant or who are breast feeding should not take any statin drug.

Muscle Tissue Damage

The symptoms are muscle aches, soreness, tenderness, or weakness. Roughly 1% to 5% of people who

take a statin experience these symptoms. This includes people taking lower doses, although low doses (10mg and 20mg) are much less likely to cause problems.

The symptoms of muscle problems (liver, too) include unexplained muscle weakness or pain, feeling very tired even though you've slept well, nausea and vomiting, stomach pain, brown or dark colored urine, and yellowing skin. *Consult your doctor immediately if you begin to have these symptoms.* Usually, the symptoms go away within days or weeks after you stop taking the drug.

Rarely, statins cause a life-threatening form of muscle breakdown called rhabdomyolysis. This can lead to permanent kidney damage and coma. One statin, cerivastatin (Baycol), was withdrawn from the U.S. market in 2001 because it caused several deaths from rhabdomyolysis.

Larger doses of statins raise the risk of muscle aches, weakening, and rhabdomyolysis. Taking a statin in combination with certain other drugs (gemfibrozil, verapamil, and niacin; check with your doctors for a list of others) can also significantly increase the risk of muscle damage and rhabdomyolysis. Research is also underway now to see if the cholesterol-lowering drug ezetimibe (Zetia) increases the risk of muscle problems or rhabdomyolysis. Some very preliminary evidence suggested this may be the case.

Other factors that may increase the risk include hypothyroidism, surgery or trauma, heavy exercise, excessive alcohol intake, and kidney or liver disease.

Liver damage

Liver damage while taking a statin is uncommon, and it is usually mild. Nevertheless, the FDA advises that all patients prescribed a statin have liver function tests before and periodically after starting treatment. Talk with your doctor about those tests.

Difference Among Statins

Overall, the statins at low doses do not differ with respect to the risks of these adverse effects. Generally, people taking 10mg or 20mg of any of the statins are at very low risk of muscle or liver problems.

However, studies in recent years have raised concerns about muscle damage associated with high doses of some of the statins. For example, one recent study found that 80mg of simvastatin caused muscle damage in nine people. Three developed rhabdomyolysis. The risk of rhabdomyolysis was higher than expected, but the three patients had other risk factors for the complication. The largest study of the safety of a statin followed 8,245 people who took generic lovastatin in doses of 20mg, 40mg, or 80mg for four years. The incidence of muscle and liver problems increased with increasing doses

Most experts believe – and the evidence so far strongly suggests – that all the statins have the potential to cause muscle problems at high doses. But until definitive studies are done, it is not clear whether some statins now on the market may pose more risk than others. As stated earlier in this report, several studies have suggested that rosuvastatin (Crestor) may pose such a greater risk. Studies are underway to clarify whether this is true or not, and in general to track the safety of statins.

Finally, studies have shown that grapefruit juice can enhance the absorption of statin drugs. While no studies have found any ill effects from this, in theory it could increase the potential for muscle and liver problems, or other minor side effects.

Age, Race, and Gender Differences

Women, people over age 65, and various ethnic groups have been under-represented in the major studies of statins. A recent review of statin studies suggested that the drugs are equally effective and safe in men, women, and people over age 65.

The benefits of statins are less certain, however, in women who have very marginally elevated LDL and do not already have heart disease. We advise those women to discuss this issue with their doctors.

Also, if you are of Asian heritage, the FDA has asked the manufacturer of the newest statin, rosuvastatin (Crestor), to do additional studies to determine the appropriate dosage of that drug in Asian-Americans. Studies indicate that Asian-Americans are more vulnerable to side effects and muscle problems if they take high doses of Crestor.

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 statin drug or dose is best for you, and which is the Best Buy Drug for you.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctors 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 many physicians) also believe that newer drugs are always or almost always better. While that's a natural assumption to make, the fact is that 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 almost always 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 half of all prescriptions in the U.S. are for generics.

As you have learned in this report, three statins are now available as 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, they may not always tell each other which drugs have been prescribed for you.
- Second, it is very common for doctors today to prescribe several medicines for you before finding one that works well or best, mostly because people vary in their response to prescription drugs.
- Third, more and more people today take several prescription medications, nonprescription drugs and supplements all at the same time. Many of these interact in ways that can be very dangerous. For example, statins interact with a blood thinning drug called warfarin, requiring the dose of warfarin to be adjusted.
- 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 list of the drugs you are taking, both prescription and nonprescription and including dietary supplements.

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* Statins

Our evaluation is based on an independent scientific review of the evidence on the effectiveness, safety and adverse effects of statins. 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 15-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of the statins 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 statins is available at <http://www.ohsu.edu/drugeffectiveness/reports/final.cfm>. (Note: This a long and technical document written for physicians.) This update of our previous statin report (June 2006) also relied on recent studies and review articles.

The prescription drug costs we site were obtained from a healthcare information company that tracks

the sales of prescription drugs in the U.S. 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 December 2006.

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 six statins
- Have a safety record equal to or better than other statins
- Have an average price for a 30-day supply that is lower than the most costly statin meeting the first two criteria, or soon will be.

The *Consumers Reports Best Buy Drugs* methodology is described in more detail in the methods section at 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 website is www.consumer.org. The magazine's website is 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.

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