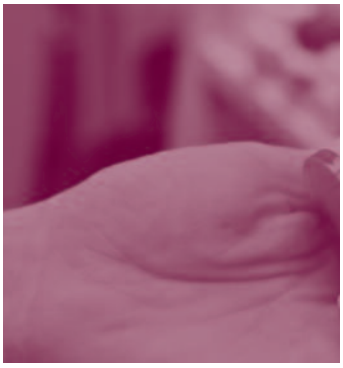
ConsumerReports® Health

# BEST BUY DRUGS™

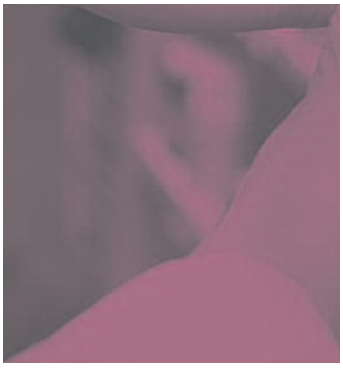
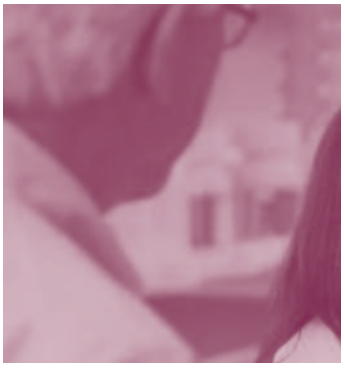
## Using Antiplatelet Drugs to Treat:

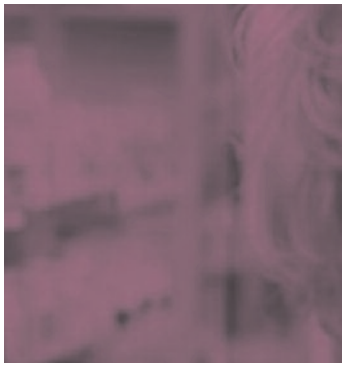
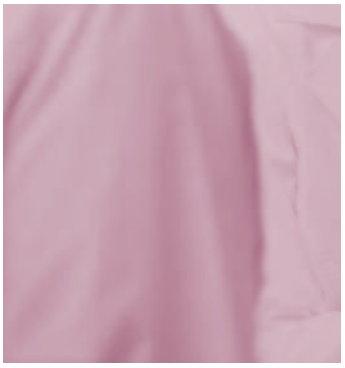
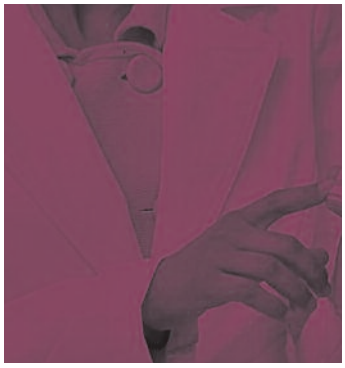
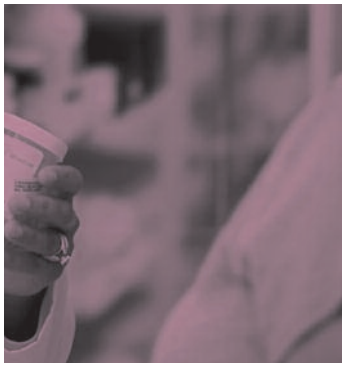
# Heart Disease, Heart Attacks, and Strokes

Comparing Effectiveness, Safety, and Price





# Our Recommendations

Antiplatelet drugs are used to lower the risk of heart attacks and strokes and to treat people who have artery blockages in their legs. They work by reducing the formation of blood clots, which can lead to heart attacks, strokes, and gangrene.

Antiplatelet medications are among the most widely used drugs in the world, primarily because aspirin is one of them. This report evaluates their use in preventing heart attacks, strokes, and premature death in people who have acute coronary syndrome (unstable angina), peripheral vascular disease, an intravascular stent, or have had a heart attack or stroke. Five antiplatelets are evaluated in this report: aspirin, a fixed combination of aspirin plus extended-release dipyridamole (Aggrenox), clopidogrel (Plavix), prasugrel (Effient), and ticlopidine (Ticlid and generic).

Taking effectiveness, safety, side effects, and cost into account, we have chosen the following as *Consumer Reports Best Buy Drugs* for people in these clinical circumstances:

- *Aspirin plus clopidogrel (Plavix)* — If you've been diagnosed with acute coronary syndrome (e.g. unstable angina) or have had a heart atttack or stent implanted.
- *Clopidogrel (Plavix)*—If you can't take aspirin and have been diagnosed with acute coronary syndrome or had a stent implanted.
- *Aspirin, aspirin plus extended-release dipyridamole (Aggrenox), or clopidogrel (Plavix)*—If you've had a stroke or ministroke (TIA).
- *Aspirin*—If you have peripheral vascular disease.

Be sure to ask your doctor about generic clopidogrel, which should become available in the spring of 2012.

*This report was published in September 2011.*

# Welcome

This report compares the effectiveness, safety, and cost of a class of medicines called antiplatelets. Your doctor might also refer to them as "blood thinning" drugs. Technically, they don't actually thin the blood; instead, they interfere with an important part of the process by which the blood clots. Namely, they decrease the clumping of blood cells called platelets. This lowers the risk that potentially harmful blood clots will form. Some people might be prone to the formation of such clots.

As is further explained below, decreasing the risk of blood clots helps prevent future heart attacks and strokes in people who have or are at high risk of heart disease, or have already had a heart attack or stroke.

Antiplatelet drugs are also used to treat people who are having a heart attack, or just afterwards, since most heart attacks are caused by clots in the arteries that feed the heart muscle itself. They are also almost always prescribed for people who have a surgical procedure called angioplasty, which unblocks arteries and is usually accompanied by the placement of a mesh tube called a stent to prop open the unblocked artery. Antiplatelet drugs are also prescribed for people who have artery blockages in their legs.

Aspirin is the best known antiplatelet drug, but there are several others. This report focuses on aspirin and four other antiplatelet medications used for preventing heart attacks, strokes, and premature death in people who have acute coronary syndrome, peripheral vascular disease, a stent, or previously had a stroke. The five medications evaluated are:

| Generic Name | Brand Name(s) | Available as a Generic Drug? |
|---|---|---|
| Aspirin[1] | Bayer, Bufferin, Ecotrin, and others[1] | Yes[1] |
| Aspirin plus extended-release dipyridamole[2] | Aggrenox | No[2] |
| Clopidogrel | Plavix | No[3] |
| Prasugrel | Effient | No |
| Ticlopidine | Ticlid | Yes |

1. Aspirin is actually a chemical called acetylsalicylic acid. The word "aspirin" was originally a brand name coined by the Bayer Company in Germany in the late 1890s. Aspirin is, of course, sold as a nonprescription drug. It is also an ingredient in dozens of nonprescription and prescription medicines.
2. Short-acting dipyridamole (Persantine) is available as a generic, but it has not been shown to reduce the risk of heart attacks or strokes, even when combined with aspirin. Long-acting dipyridamole is not currently available in generic form.
3. The generic is expected to become available in the spring of 2012.

Aspirin is used to relieve pain and headaches and reduce fevers, but doctors also prescribe it to reduce the risk of heart attack and stroke in people who have heart disease and people with an elevated risk of heart attack or stroke—such as those who smoke, have high blood pressure, high cholesterol, diabetes, or are overweight (For more on that, visit our website: http://www.consumerreports.org/health/conditions-and-treatments/heart-health/prevent-heart-disease/consider-low-dose-aspirin.htm). Aspirin is by far the most widely used antiplatelet drug.

Three of the other antiplatelet drugs were approved by the Food and Drug Administration (FDA) in the 1990s—Ticlid in 1991, Plavix in 1997 and Aggrenox in 1999. Effient was approved in 2009. Only Ticlid is available as a low-cost generic.

There are two other antiplatelet drugs—an older medication called cilostazol (Pletal) and a newer drug, Brilinta (ticagrelor), which was approved by the FDA as this report was being prepared for publication—that were not included in the analysis by the Oregon Health & Science University's Drug Effectiveness Review Project that forms the basis of our report. So we do not evaluate them or how they compare to the other antiplatelet drugs. We recommend avoiding Brilinta until more is known about it. It is a new drug, so it does not have the long track record that some of the other antiplatelet drugs do. Its label carries a black box warning that its effectiveness is reduced if people also take more than 100 mg of aspirin per day.

This report is part of a *Consumer Reports* project to help you find medicine that is safe and effective and gives you the most value for your health-care dollar. To learn more about the project and other drugs we have evaluated, go to ConsumerReportsHealth.org/BestBuyDrugs.

Our analysis of the antiplatelet drugs is based on a thorough review of the medical research. More than 1,700 studies and research articles were screened. Of those, 39 studies, including clinical trials, observational studies and systematic reviews, were focused on in the analysis that forms the basis for this report.

Antiplatelet drugs are just one type of medicine used today to treat people with heart disease and those who have had a heart attack or stroke. They are usually combined with other medications, nondrug treatments, and lifestyle and dietary changes. For lifestyle changes and other strategies that can help keep your heart healthy, check out our free guide on preventing heart disease: http://www.consumerreports.org/health/conditions-and-treatments/heart-health/prevent-heart-disease/overview.htm.

Antiplatelet drugs should not be confused with other medications often referred to as anticoagulants. Those include heparin, enoxaparin (Lovenox), and warfarin (Coumadin and generic). Anticoagulants and antiplatelet drugs both reduce blood clotting, but they are used for different circumstances. Anticoagulants are more likely to be prescribed to treat or prevent blood clots in the leg veins or lungs, in people who have inherited blood clotting disorders, or in patients who have a heart rhythm disturbance known as atrial fibrillation. Heparin is usually used in hospitals, and only rarely is used as a prescription drug to be taken at home.

Anticoagulants should be used with greater caution and care than the antiplatelet drugs, as your doctor will tell you. When antiplatelet drugs are used together with anticoagulants, both patients and doctors should be aware that there is an increased risk of bleeding.

This report was published in September 2011.

# What are Antiplatelet Drugs and Who Needs Them?

Antiplatelet drugs prevent blood cells called platelets from clumping together and forming a blood clot. Platelets clump together if you're bleeding—this is a normal part of blood clotting that stops you from bleeding endlessly, so you wouldn't want to stop this normal process altogether.

But in people whose arteries have narrowed from atherosclerosis—the "hardening of the arteries" that is the basis of coronary artery disease and peripheral artery disease (in the legs and neck, for example)—blood clumping and clotting can become dangerous.

Blood clots are especially dangerous when they get hung up in an area of an artery where a build-up of fat and cholesterol has occurred. Such areas are called plaques. When platelets pass over a plaque with a roughened or eroded surface, they are triggered to clump together as if it were an injury. And plaques can rupture, attracting platelets to the site, initiating the formation of a clot.

A heart attack can occur if this happens in a narrowed artery serving the heart muscle, because the artery gets blocked completely or almost completely, starving the heart muscle of oxygen.

When a clot forms and gets hung up on a plaque in a narrowed artery that leads to or is located in the brain, a stroke or mini-stroke (called a transient ischemic attack or TIA) can occur. If that happens in a narrowed artery in a leg, the affected limb can suddenly become painful and numb, and the muscle and other tissue can be damaged.

Antiplatelet drugs help prevent these potentially deadly events by lowering the risk of clot formation at the site of plaques. Your doctor is most likely to prescribe an antiplatelet drug if he or she diagnoses you with coronary artery disease (often just called heart disease), or if you have had a heart attack, stroke or TIA, or problems related to poor blood supply to your legs.

The hallmark symptom of coronary artery disease is a type of chest pain called angina. But you can have other symptoms also. They include a feeling of tightness or pressure in the chest, shortness of breath, nausea, and sweating. Your doctor will also do some tests to confirm the diagnosis. See the box on this page for the telltale symptoms of a mini-stroke as well.

### Symptoms of Coronary Artery Disease or Heart Attack

**Might be stable or worsen over time. See a doctor right away, go to an emergency room, or call 911.**

- Chest pain (angina)
- Pressure and/or feeling of tightness in chest
- Shortness of breath
- Nausea, vomiting
- Sweating, dizziness
- Pain or discomfort in upper body, such as arms, jaw, shoulder, or neck

### Symptoms of a Mini-Stroke

**Usually come on suddenly and noticeably. Might pass in a few minutes. See a doctor right away, go to an emergency room, or call 911.**

- Numbness or weakness of one side of the face, an arm, or a leg
- Trouble speaking or understanding
- Difficulty walking
- Confusion or loss of coordination
- Sudden loss of vision in one or both eyes
- Sudden severe headache

If your doctor diagnoses you with heart disease, he or she is also highly likely to advise lifestyle changes—such as quitting smoking, losing weight, or getting more exercise—to help reduce your risk of a heart attack or stroke. You might also be prescribed medicine to lower high blood pressure, elevated cholesterol levels, and the work load on your heart.

Aspirin is usually recommended for people who have had a heart attack, a mini-stroke, a full stroke (the kind caused by a clot), or those with heart disease—provided they can safely take it. Aspirin is also prescribed for people who have not yet been diagnosed with heart disease, but have risk factors (family history, smoking, high blood pressure or

cholesterol) for heart attack or stroke. About half of the people who have a heart attack each year have no overt signs of heart disease, such as prior chest pain. (See "Aspirin Use and Your Heart Risk" on page 7.)

Aspirin is the primary first-choice antiplatelet drug.

## Six Groups Who Might Need an Antiplatelet Drug

It's useful to divide the population of people who need aspirin or another antiplatelet drug into six groups:

- People who have risk factors that make them high risk but no diagnosed heart disease
- People who have heart disease with angina that is "stable"
- People who have heart disease with angina that is "unstable" or who are having a heart attack—these are also called acute coronary syndrome
- People who have had angioplasty, a stent placed in a heart blood vessel, or bypass surgery (a procedure to open blocked arteries or bypass the blockage with a graft)
- People who have a mini-stroke (TIA) or stroke
- People who have peripheral artery disease or poor blood circulation

Taking each of those one by one:

- People who have risk factors but have not been diagnosed with heart disease benefit from aspirin if they can safely tolerate it. Only rarely would people in this group be prescribed one of the other antiplatelet drugs. Aspirin treatment, which aims to prevent a first heart attack or stroke, is often referred to by doctors as "primary prevention."
- People whose chest pain (angina) follows a predictable pattern—triggered by exercise or other activities that increase the exertion of the heart or emotional distress and goes away with rest—are considered to have so-called "stable angina." They will be assessed for aspirin treatment, and prescribed it if there are no reasons not to take it. Such people are probably taking other medicines as well, but only rarely would they be prescribed two antiplatelet drugs. Aspirin is considered sufficient.
- In contrast, if a person with previously "stable" chest pain and other symptoms starts to have more frequent and severe symptoms or pain when they're just sitting around and not exerting themselves, they are considered to have "unstable angina." People with this type of angina are at much greater risk of a heart attack. Indeed, unstable angina can mean that a heart attack is imminent because of a dangerously narrowed or completely blocked artery.

  Doctors also refer to people in this state as having "acute coronary syndrome" (ACS). ACS is considered a medical emergency requiring immediate treatment and possible hospitalization.

  Not surprisingly, then, your treatment is more complicated. Specifically, your doctor might recommend an immediate diagnostic procedure called an angiography to locate artery blockages and possibly treat them. This involves placing a thin, flexible tube into a blood vessel in your groin, and then snaking it up to your heart to visualize the coronary arteries and find blockages.

  If just one or two blockages are found, the doctor can activate a tiny balloon near the end of the tube and compress the blockage to open the artery. This procedure is called angioplasty. In addition, the doctor can then choose to insert a tiny wire-mesh tube, called a stent, to prop open the artery.

  If a lot of severe blockages are found, your doctor might recommend coronary artery bypass surgery.

  People with unstable angina and/or acute coronary syndrome will be assessed for aspirin treatment. Before hospitalization, they might be prescribed aspirin alone. But once hospitalized or treated in an emergency room, they will almost always get other medicine, including a second antiplatelet drug and possibly one of the anticoagulants, such as heparin.
- Patients who have coronary angioplasty and bypass surgery are also commonly prescribed antiplatelet drugs.

## Aspirin Use and Your Heart Risk

Aspirin lowers the risk of a repeat attack or stroke by about a third in people who have already had a heart attack or stroke. Put another way, it prevents two to three heart attacks or strokes for every 100 people who take it over a three-year period.

As a result, the American Heart Association and the American College of Cardiology currently recommend a daily aspirin pill (81 mg to 325 mg) for anyone who has had a heart attack or a stroke and can safely take the medicine (More about that below).

Things get trickier when aspirin treatment is considered for people who have not been diagnosed with heart disease or haven't had a heart attack or stroke, but are considered to be at high risk of them. This includes people who smoke, don't exercise, or are overweight, as well as those with high blood pressure, high cholesterol, or diabetes. Many doctors also include in this at-risk group all men 55 and older, postmenopausal women, and anyone who has a family history of early-age (under 60) heart attacks and/or strokes.

Studies show aspirin lowers the chance of a heart attack or stroke for such people. But the best time for them to start taking aspirin, and at what dose, is less clear. The benefits of aspirin for this group should be weighed carefully against the risks it poses. Namely, aspirin can cause bleeding in the stomach—even at low doses—when taken every day. It can also cause increased bleeding in menstruating women. Bleeding in the brain is another risk. It is less common, but it's of concern because it raises the risk of a hemorrhagic stroke.

Because there is no precise way to judge or calculate the benefits vs. risks, medical groups and government agencies recommend that this be decided on a case-by-case basis for people with one or more heart-disease risk factors. That recommendation goes as well for people who don't have risk factors but are interested in the heart protective effect of daily aspirin. Your doctor might concur that a daily low-dose aspirin pill (81 mg) is worth it.

But we advise against taking aspirin everyday on your own before talking with your doctor about the potential risks and benefits.

In general, people who have multiple risk factors for heart disease (for example, if they smoke, have diabetes, and don't exercise) stand to benefit more from aspirin treatment (making the risk of side effects worth it) than people who have no risk factors or only one.

Non-emergency angioplasty surgery and the placement of stents—a procedure known as percutaneous coronary intervention—is controversial for people who do not have acute symptoms, like chest pain, or who have not had a heart attack or have not been diagnosed with unstable angina. PCI is an invasive, expensive procedure that carries risks, such as infections, bleeding and other complications. For people who do not have the symptoms or conditions listed above the procedure may not be needed, and they might do better by being treated first with various medications, including antiplatelet drugs. An analysis in the July 6, 2011 issue of the Journal of the American Medical Association found that only about half of the more than 144,000 PCI procedures in U.S. hospitals involving people who did not have a heart attack, high-risk unstable angina, or other acute symptoms were appropriate.

So if your doctor recommends angioplasty and stents, ask whether an antiplatelet and other medications should be tried first. Depending on your particular situation, it might make sense to talk about the risks of antiplatelets up front and factor that into your decision about undergoing angioplasty and stent place-

ment. For more detailed information about this issue, see http://www.consumerreports.org/health/conditions-and-treatments/heart-health/heart-disease-treatment/angioplasty-procedure.htm

If you undergo angioplasty and have a stent implanted, you might need to take two antiplatelet drugs to reduce the risk of blood clots forming inside the stent while it heals. A blood clot that forms inside the stent can cause a major heart attack and this risk is significantly reduced by taking two antiplatelet drugs like aspirin and clopidogrel or aspirin and prasugrel. Studies have found that when people took two antiplatelet drugs after stent placement for six months compared to one month, they were less likely to have subsequent blood clots and heart attacks and there was no significant increase in bleeding risk. At eight months, there is probably still a benefit but the risk of bleeding is also higher. And, if people take antiplatelet drugs for one year, there is an increased risk of a serious bleeding episode and it was less likely there was a benefit of preventing blood clots and heart attacks.

The upshot: Many who undergo stent placement will probably benefit from taking two antiplatelet drugs for six months or more, though exactly how long has yet to be determined. Current recommendations from cardiology societies advise dual antiplatelet treatment be taken for 12 months after undergoing stent placement, but the best data are for six to nine months.

If you have had a heart attack, it's likely you have also had either angioplasty, stenting, or bypass surgery, so the above discussion applies: You will probably be prescribed two antiplatelet drugs.

- You will also be prescribed at least one and potentially two antiplatelet drugs if you've had a mini-stroke, or stroke.

  Strokes are a bit more complex. About 85 percent of them are caused by blood clots and are treated with an antiplatelet drug. But about 15 percent are instead caused by the rupture of a blood vessel and bleeding in or around the brain. These are known as hemorrhagic strokes. Antiplatelet drugs are not a treatment for those types of strokes because they can make matters worse.

  So before you take an antiplatelet drug for a stroke or TIA, a scan of your brain will be done to rule out bleeding.

- Finally, your doctor may prescribe an antiplatelet drug if you have poor blood circulation in your legs (or one leg) or evidence of artery narrowing or blockages in your legs. This condition—known as peripheral vascular disease—afflicts eight to 12 million people in the U.S. and increases the risk of heart disease and artery blockages elsewhere in the body. It is often characterized by calf pain that occurs when walking. But in those without typical symptoms, this condition can be detected through a decrease in blood pressure in the leg.

## Side effects and safety

Like all drugs, antiplatelet medications can cause side effects. While most are generally mild, some can be dangerous and even life-threatening. Notably, all antiplatelet drugs increase the risk of bleeding in the gastrointestinal tract and brain. (See the box on the next page.)

Clopidogrel (Plavix), prasugrel (Effient) and ticlopidine (Ticlid) have been linked to a condition known as thrombotic thrombocytopenic purpura (TTP). In people with TTP, small blood clots made of platelets form suddenly throughout the body, lowering the number of circulating blood cells. This can cut off the blood supply to organs, especially the kidneys and brain. The condition can be life-threatening and requires immediate medical attention. Symptoms include fevers, difficulty thinking clearly, and easy bruising.

For clopidogrel (Plavix) and prasugrel (Effient), the risk of TTP is very small, and not clearly established. But people who take ticlopidine (Ticlid and generic) have a risk for TTP that's much higher than those taking clopidogrel or prasugrel. For that reason, the FDA requires that Ticlid have a black box warning on its label—the strongest warning that the FDA can issue—citing the risk of TTP. The warning also cautions that Ticlid has been associated with two other blood-related conditions: neutropenia (low white blood cell count) and aplastic anemia (when the body's bone marrow doesn't make enough new blood cells, which can lead to heart problems and even death).

## Side Effects of Antiplatelet Drugs

**Minor; usually go away over time**

- Headaches
- Diarrhea
- Nausea
- Flatulence
- Dizziness

**Rarer but not minor; can be dangerous or even life-threatening. Not all antiplatelets can cause all of these. See a doctor immediately or go to an emergency room if they occur.**

- Rash
- Stomach bleeding
- Nose bleeding
- Bleeding in the brain
- Excessive weakness
- Stomach pain
- Yellowing of the skin
- Vomiting

**Severe and possibly life-threatening; linked to selected newer antiplatelets, not aspirin**

- Thrombotic thrombocytopenic purpura (TTP)—the development of tiny blood clots
- Neutropenia—low white blood cell count
- Aplastic anemia—when body stops making new red blood cells

The risk of TTP with ticlopidine is estimated to be one in 2,000 to 4,000 people who take it. A similar number are at risk for aplastic anemia. The danger of getting any of the three conditions—TTP, neutropenia, and aplastic anemia—is highest during the first three months of taking ticlopidine. During that time, people should see their physician regularly and get lab tests to monitor for problems. Stop taking the drug if there are signs of serious side effects.

Aggrenox contains aspirin, so it poses some of the same risks as aspirin (primarily, the risk of stomach bleeding). The drug has also been associated with worsening chest pain in people who have unstable angina or those who have had a recent heart attack. In addition, Aggrenox can decrease the beneficial effects of the following medications: ACE inhibitors, anticonvulsants, beta-blockers, cholinesterase inhibitors, and diuretics.

Clopidogrel and ticlopidine can also interact adversely with other medicines. Those include: antacids, digoxin, fluvastatin, non-steroidal anti-inflammatory drugs, oseltamivir (Tamiflu), tamoxifen, theophylline, and warfarin.

Antiplatelet drugs can interact with some dietary supplements as well, in ways that can be dangerous. Be sure to tell your doctor about any other medications and supplements or herbs you are taking.

# Choosing an Antiplatelet Drug — Our *Best Buy* Picks

Tables 1 and 2, on pages 11 and 12, respectively, summarize the evidence for antiplatelet drugs. Although no studies have directly compared all five drugs, enough studies have compared one antiplatelet to another to allow us to make recommendations on their use in various clinical circumstances.

The evidence is strongest for aspirin. Dozens of studies support the use of aspirin in patients needing a blood thinner. And, as indicated earlier, aspirin is the initial drug of choice for many people, as long as they're not allergic and don't suffer from stomach bleeding or ulcers.

Aspirin is also very inexpensive. So anyone who can potentially benefit can probably afford it. In fact, as evidence of aspirin's benefits mounted over the last 20 years, many observers have noted that it's interesting that one of the cheapest medicines in the world is so effective against one of the major killers around the world—heart disease.

Aspirin is not for everyone though. Indeed, as indicated in the previous section, the use of the antiplatelet drugs is complicated by a common practice of prescribing a second blood thinner in addition to aspirin for many people.

To help guide you and your doctor, Table 2 on page 12 lists antiplatelet treatment choices. It compares the five drugs and chooses a "best treatment" for different clinical circumstances. For example, studies have found that aspirin or clopidogrel (Plavix) plus aspirin are the best options for people who have heart disease without symptoms or stable angina, while aspirin plus clopidogrel (Plavix) is the best option for people who have acute coronary syndrome (e.g. unstable angina or heart attack). If you cannot take aspirin, then clopidogrel alone is the next best option.

Studies have shown very clearly that the combination of aspirin plus clopidogrel is far more effective at preventing heart attacks than aspirin alone in people who have had a stent implant.

The evidence is a bit murky when it comes to preventing a second stroke in people who have already had one. Among the three newer antiplatelets, Aggrenox is the only one found to be significantly more effective than aspirin alone for preventing a second stroke in such people. But, when directly compared to one another in a head-to-head trial, researchers found that Aggrenox might not work as well as clopidogrel in preventing a second stroke and might have a higher risk of major bleeding. And none of the drugs have been proven better than aspirin alone for preventing death in people who have already suffered a stroke.

## Safety and cost issues

Your choice of an antiplatelet drug will also depend on you and your doctor's assessment of the risk it poses. Also, if you are allergic or intolerant to aspirin or at higher risk for gastrointestinal bleeding you might need to use clopidogrel.

As discussed in the last section, the drug ticlopidine (Ticlid and generic) poses unique risks greater than those of the other antiplatelet drugs. For this reason, we advise against its use at all since there's no evidence it has superior effectiveness compared with the other antiplatelet drugs.

Cost considerations are an issue still with this class of drugs. Because aspirin is so cheap, it is recommended liberally by many doctors. In contrast, because the other medicines are substantially more expensive, both doctors and patients should be sure that their use is warranted compared to aspirin alone. Fortunately for consumers, clopidogrel (Plavix) is expected to become available—once again—in the spring of 2012. (For a short period of time, generic clopidorel was available in 2006, but the company that makes Plavix promptly sued and distribution of the generic was halted in 2007.)

| Table 1. Summary of the Evidence for Antiplatelet Drugs | | | | | |
|---|---|---|---|---|---|
| **Brand name(s)** | **Generic name** | **Effective in preventing a heart attack or death in people with acute coronary syndrome?** | **Effective in preventing a stroke in people who have had a previous stroke?** | **Effective in preventing death in people with peripheral vascular disease?** | **Increased risk of internal bleeding when taken with aspirin?** |
| Bayer, Bufferin, Others | Aspirin | Yes | Yes | Yes | NA |
| Aspirin plus Plavix | Aspirin plus clopidogrel | Yes | No evidence | Probably | Yes |
| Aggrenox | Aspirin / extended-release dipyridamole | No evidence | Yes | No evidence | Yes |
| Effient | Prasugrel | No evidence | No evidence | No evidence | Yes |
| Effient plus Aspirin | Prasugrel plus aspirin | Yes (only after stent placement ) | No evidence | No evidence | Yes |
| Plavix | Clopidogrel | Yes | Probably | Probably | Yes |
| Ticlid | Ticlopidine | No evidence | Maybe | No evidence | Yes |
| Ticlid plus Aspirin | Ticlopidine + Aspirin | Yes (only after stent placement) | No evidence | No evidence | Yes |

NA = Not applicable

Taking effectiveness, safety, side effects, and cost into account, we have chosen the following as *Consumer Reports Best Buy Drugs* for people in these clinical circumstances:

- *Aspirin plus clopidogrel (Plavix)* – If you've been diagnosed with acute coronary syndrome (e.g. unstable angina or have had a heart attack), or if you've had a stent implanted.
- *Clopidogrel (Plavix)*–If you can't take aspirin and have been diagnosed with acute coronary syndrome or had a stent implanted.
- *Aspirin, aspirin plus extended-release dipyridamole (Aggrenox), or clopidogrel (Plavix)*–If you've had a stroke or ministroke (TIA).
- *Aspirin*–If you have peripheral vascular disease.

If you are diagnosed with peripheral vascular disease, your doctor will likely prescribe aspirin first. If you then have another blood clot in your legs, he or she might switch you to one of the other blood-thinning drugs, prescribe another one alongside aspirin, or consider an anticoagulant drug.

## Differences due to age, race, gender or health status

No studies have directly compared the effectiveness of the antiplatelet drugs in older vs. younger people, men vs. women, or people of different races or ethnic backgrounds. However, there is some evidence that suggests there is no net benefit for patients 75 years old or older using prasugrel.

Some studies have evaluated the drugs in people with specific health conditions – such as those with

## Table 2. Your Treatment Choices With Antiplatelets

| Condition/Your Health Status | Best Treatment [1] | Best Treatment if You Can't Take Aspirin [2] | Less Effective, Less Safe, or No Evidence | Comments or Cautions |
|---|---|---|---|---|
| **Have Acute Coronary Syndrome (also called unstable angina or had a heart attack)[3]** | Aspirin + clopidogrel (Plavix) | Clopidogrel (Plavix) | Prasugrel (Effient), Ticlopidine, Aggrenox | Aspirin + clopidogrel shouldn't be taken by people at higher risk of stomach bleeding or ulcers. |
| **Had a Stent Implanted** | Aspirin + clopidogrel (Plavix) [4] | Clopidogrel (Plavix) | Prasugrel (Effient), Ticlopidine, Aggrenox | Strong evidence for benefit of the combination of drugs. Prasugrel is similar to clopidogrel for reducing all-cause and cardiovascular death with a slightly higher risk of bleeding. |
| **Have Had a Stroke or Mini-Stroke (TIA)** | Aggrenox or Clopidogrel (Plavix) or aspirin | Clopidogrel (Plavix)[5] | Prasugrel (Effient), Ticlopidine | Aspirin alone has been found less effective than Aggrenox and clopidogrel is similar to Aggrenox. |
| **Peripheral Vascular Disease[6]** | Aspirin | Clopidogrel (Plavix) | Prasugrel (Effient), Aggrenox, Ticlopidine | Evidence suggests aspirin and clopidogrel are similar. |

1. "Best Treatment" indicates best initial treatment for the majority of patients. Individual circumstances vary, however, and your doctor might advise another treatment course for good clinical reasons.
2. Some people are allergic to aspirin or are particularly sensitive to its adverse effects on their stomachs, with a resultant higher risk of stomach bleeding and ulcers.
3. Acute coronary syndrome indicates a heart attack may be imminent.
4. Except for people who are at higher risk of internal bleeding, for example from stomach ulcers. The combination in some people adds to that risk. It can also add to the risk of bleeding in the brain, which can trigger a kind of stroke called a hemorrhagic stroke.
5. Not strong evidence for clopidogrel in preventing secondary strokes; aspirin second best choice if you can take it.
6. Peripheral vascular disease mostly involves blood clots and vein blockages in the legs. This can occur in one leg or both legs.

diabetes, high blood pressure, or a history of previous heart surgery. There is some evidence suggesting there was additional harm of using prasugrel after stent placement for patients who also had a previous stroke or transient ischemic attack. All of the other antiplatelet drugs helped patients with existing health conditions, but they appeared to work no better or worse than for people without those conditions.

There has been a lot of interest in using genetic testing to determine which people might respond better to clopidogrel and/or other antiplatelet drugs, but the available studies to date do not clearly show whether this type of testing leads to better outcomes.

## Table 3: Costs of Antiplatelet Drugs

| Generic Name and Dose | Brand Name [1] | Frequency of Use Per Day [2] | Average Monthly Cost [3] | *Best Buy* Indication |
|---|---|---|---|---|
| CR BEST BUY Aspirin tablet 81 mg-325 mg | Bayer, Bufferin, Others, and Generic | One | $1 [5] | Stroke or mini-stroke, Peripheral Vascular Disease. Also acute coronary syndrome or after stent implantation when used together with Plavix. |
| CR BEST BUY Aspirin/dipyridamole sustained-release capsule 25 mg/200 mg | Aggrenox | Two | $247 | Stroke or mini-stroke |
| CR BEST BUY Clopidogrel tablet 75 mg [4] | Plavix | One | $214 | Acute coronary syndrome or after stent implantation when combined with aspirin. Plavix alone is a Best Buy for those conditions if you can't take aspirin. |
| Prasugrel tablet 10 mg | Effient | One | $222 | |
| Prasugrel tablet 5 mg | Effient | One | $231 | |
| Ticlopidine tablet 250 mg | Generic | Two | $64 | |

1. "Generic" indicates that this drug is sold as a generic.
2. Frequency of use reflects usual frequency; some products might be used more or less frequently.
3. Prices (except for aspirin) reflect nationwide retail average for April 2011, rounded to the nearest dollar; prices are derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Pharma Solutions, which is not involved in our analysis or recommendations.
4. Generic clopidogrel is expected to become available the spring of 2012.
5. Average aspirin prices were calculated by *Consumer Reports Best Buy Drugs* using prices obtained from seven online drugstore retailers, including: Costco.com, CVS.com, Drugstore.com, Familymeds.com, Healthwarehouse.com, Kroger.com, and Target.com.

## Talking With Your Doctor

It's important for you to know that the information we present in this report is not meant to substitute for a doctor's judgment. But we hope it will help you and your doctor arrive at a decision about which antiplatelet drug or dose is best for you, if one is warranted, and which will give 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 doctors. Also, studies have found that doctors don't routinely take price into account when prescribing medicines. So unless you bring it up, your doctor might assume that cost is not a factor for you.

Many people (including physicians) think that newer drugs are better. While that's a natural assumption to make, it's not necessarily true. Studies consistently find that many older medicines are as good as—and in some cases better than—newer medicines. Certain older drugs can be thought of 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 drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer vs. older medicines, including generic drugs.

Prescription medicines go "generic" when a company's patents on them 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're not lesser quality drugs. Indeed, most generics remain useful even many years after first being marketed. That is why more than 60 percent of all prescriptions in the U.S. today 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, they might not be aware of medications the others have prescribed for you.
- Second, since people differ in their response to medications, it's very common for doctors today to prescribe several for a person before finding one that works well or best.
- Third, many people take several prescription medications, nonprescription drugs, and dietary supplements at the same time. They can interact in ways that can either reduce the benefit you get from the drugs or be dangerous.
- Fourth, the names of prescription drugs—both generic and brand—are often difficult 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 it with your doctors.

And always be sure that you understand the dose of the medicine being prescribed and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at a pharmacy or get it by mail, make sure the dose and the number of pills per day on the container match the amount your doctor told you to take.

## How We Picked the *Best Buy* Antiplatelet Drugs

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

A synopsis of DERP's analysis of antiplatelet drugs 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 antiplatelet drugs is available at http://www.ohsu.edu/drugeffectiveness/reports/final.cfm. (Note: This is a long and technical document written for physicians.)

The prescription drug costs we cite 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 April 2011.

*Consumer Reports* selected the *Best Buy Drugs* using the following criteria. The drug had to:

- Be as effective or more effective than the other antiplatelet drugs
- Have a safety record equal to or better than other antiplatelet drugs

Cost was less of a factor in assessing this class of medicines because aspirin is such an inexpensive medicine, there are few drugs in this category (and thus much less choice), and compelling evidence shows two of the more expensive medicines are beneficial in certain medical circumstances.

The *Consumer Reports Best Buy Drugs* methodology is described in more detail in the methods section at ConsumerReportsHealth.org/BestBuyDrugs.

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# About Us

Consumer Reports, 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 create a fair marketplace. Its website is www.ConsumerReports.org.

*Consumer Reports Best Buy Drugs*™ is a public-education project administered by Consumer Reports. These materials are made possible from a grant by the state Attorney General Consumer and Prescriber Education Grant Program, which is funded by the multistate settlement of consumer-fraud claims regarding the marketing of the prescription drug Neurontin.

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We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Best Buy Drugs* website is accurate and describes generally accepted clinical practices. If we find an error or are alerted to one, we will correct it as quickly as possible. But Consumer Reports and its authors, editors, publishers, licensers, and 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 ConsumerReportsHealth.org/BestBuyDrugs for further information.

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