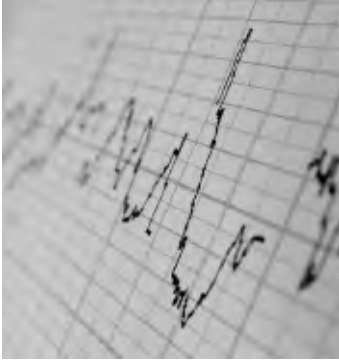


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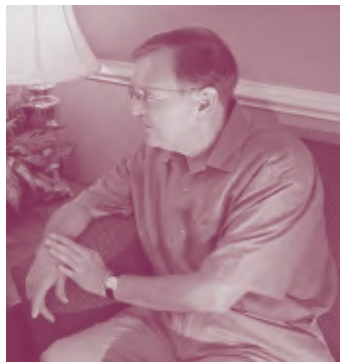
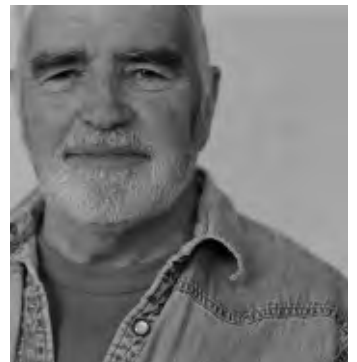
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Treating Heart Disease, Heart Attack, and Stroke:

The Antiplatelet Drugs

Comparing Effectiveness, Safety, and Price



Our Recommendations

Medicines known as antiplatelets are among the most widely used in the world, primarily because aspirin is one of them. Three newer antiplatelets – sometimes called “superaspirins” – are available. They are Aggrenox, ticlopidine (Ticlid), and clopidogrel (Plavix).

These medicines are used to lower the risk of heart attack and stroke under a variety of circumstances. They are highly effective in doing so. For example, in people who have had a heart attack, they can lower the risk of a repeat attack by about 35 percent. The antiplatelets are also used to treat people who have artery blockages in their legs.

The antiplatelet medicines work by decreasing blood clotting, which evidence now shows is directly linked to heart attack and stroke risk.

Taking the evidence for 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* – if you have risk factors for heart attack and stroke (such as high blood pressure, smoking, diabetes, and/or high cholesterol) but have not been diagnosed with heart disease or had a heart attack, stroke, or mini-stroke (also known as a transient ischemic attack, or TIA)
- *Aspirin* – if you have been diagnosed with heart disease and so-called “stable” angina
- *Clopidogrel (Plavix)* – if you have been diagnosed with heart disease, have stable angina but can not take aspirin
- *Aspirin + clopidogrel (Plavix)* – if you have what is known as “unstable” angina or acute coronary syndrome, have had a heart attack, or have had angioplasty and a stent implanted in the last year
- *Aggrenox* – if you have had a stroke or mini-stroke

It’s not possible to choose a *Best Buy* drug for people with artery blockages in their legs. Too few studies have compared the antiplatelet drugs in the treatment of this condition. However, your doctor is likely to start treating you with aspirin if you have this condition.

Be sure to ask your doctor about generic clopidogrel, although availability of this drug is in limbo due to patent litigation.

This report was released and last updated in April 2007.

Welcome

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

As is further explained below, it turns out that decreasing the risk of blood clots is one very important way to 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. And these medicines are now almost always prescribed for people who have a surgical procedure called angioplasty that unblocks arteries, usually accompanied by placement of a device (called a stent) to prop open the unblocked artery. Blood thinners are also prescribed for people who have artery blockages in their legs.

There are several different kinds of antiplatelet drugs. Notably, these include plain-old everyday aspirin. This report will focus on aspirin and several newer antiplatelet medications that are sometimes called “superaspirins.” The four drugs we evaluate 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	Yes ³
Ticlopidine	Ticlid	Yes

1. Aspirin is actually a chemical called acetylsalicylic acid. The word “aspirin” was originally a brand name for that chemical 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 (Persantin) is available as a generic, but it has not been shown to reduce the risk of heart attack or stroke, even when combined with aspirin. Long-acting dipyridamole is not currently available in generic form.

3. Clopidogrel became available as a generic in August 2006. A legal dispute over the patent on the brand version, Plavix, threatens to disrupt the supply of the generic in 2007.

These medicines are taken by millions of Americans every day. Aspirin is, of course, used as a pain and headache reliever and fever reducer. But it is also now widely prescribed to people who have heart disease and people judged by their doctors to be at elevated risk of heart attack or stroke – such as people with high blood pressure, high cholesterol, or who smoke, have diabetes or are overweight. It is by far the most widely used antiplatelet drug.

The other three medicines were approved by the Food and Drug Administration (FDA) in the 1990s – Ticlid in 1991, Plavix in 1997 and Aggrenox in 1999. Ticlid and Plavix are available as lower-cost generics. Generic Plavix – clopidogrel – is the subject of an on-going court battle, however, the ramifications of which are discussed below.

This report is part of a Consumers Union® and *Consumer Reports*® project to help you find medicines that are safe and effective and give you the most value for your health care dollar. To learn more about the project and other drugs we have evaluated, and to get price updates, go to www.CRBestBuyDrugs.org.

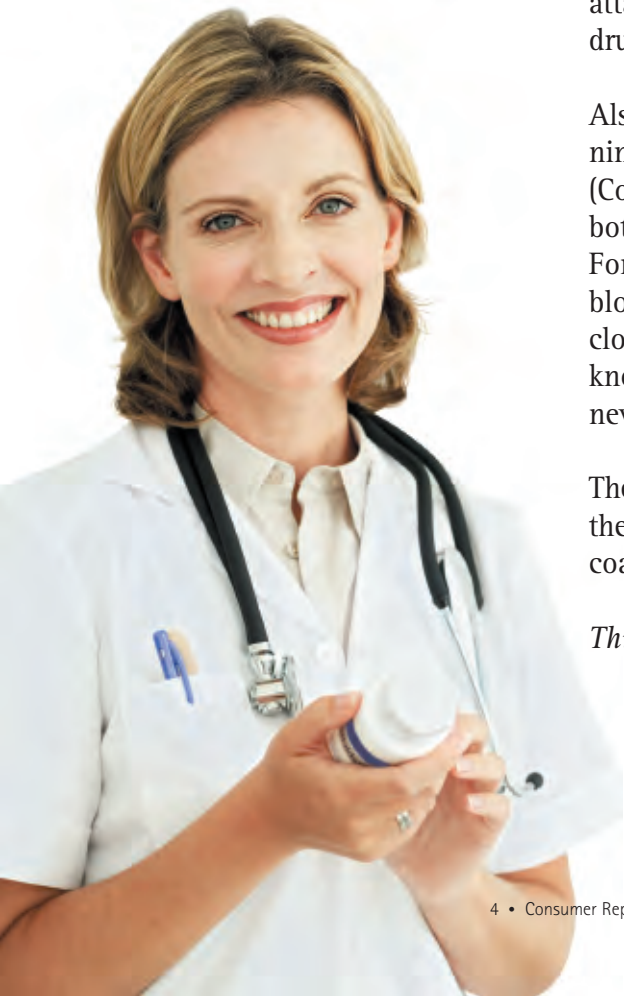
Our analysis of the antiplatelet drugs is based on a thorough review of the medical research. Just over 4,500 studies and research articles conducted over the past 20 years were screened. Of those, however, only 39 directly compared the drugs to each other in the treatment of patients. It is those studies that form the basis for this report.

Please note that the antiplatelet drugs are just one type of medicine used today to treat people with heart disease, or people who have had a heart attack or stroke. They are typically combined with other medications, non-drug treatments, and lifestyle and dietary changes.

Also, the antiplatelet drugs should not be confused with other blood-thinning drugs, often referred to as anticoagulants. These include warfarin (Coumadin), heparin, and enoxaparin (Lovenox). The two types of drugs both reduce blood clotting, but they are used under different circumstances. For example, the anticoagulants are more likely to be prescribed to treat 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 exclusively used in hospitals, and never as a prescription drug to be taken at home.

The anticoagulant drugs must be used with greater caution and care than the antiplatelets, as your doctor will tell you if he or she prescribes an anticoagulant instead of an antiplatelet drug.

This report was released and last updated in April 2007.



What are Antiplatelet Drugs and Who Needs Them?

Very simply, the antiplatelet drugs work by decreasing the clumping together of blood cells called platelets.

Platelets clump together at certain times normally. For example, if you suffer a cut, platelets are triggered to clump and this initiates the process of blood clotting. This 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, for example) – blood clumping and clotting can become dangerous.

Blood clots are especially dangerous when they get hung up in 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. Also, plaques can rupture, attracting platelets to the site and the initiation of a clot.

If this happens in a narrowed artery serving the heart muscle, a heart attack can occur as the artery gets blocked totally (or near totally), starving the heart muscle of oxygen.

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

The antiplatelet drugs help prevent all these potentially deadly events by lowering the risk of clot formation at the site of plaques.

Your doctor is most likely to consider and prescribe an antiplatelet drug if you have been diagnosed with coronary artery disease (often just called heart disease), 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 other symptoms can occur. These 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 tell-tale symptoms of a mini-stroke as well.

Symptoms of Coronary Artery Disease or Heart Attack

May 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. May 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, one arm, or one 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 you are diagnosed with heart disease, your doctor 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 may also be prescribed medicines to lower blood pressure, cholesterol, and the work load on your heart.

Aspirin is usually recommended for all people diagnosed with heart disease who can safely take it. It is also almost universally prescribed for people who have had a heart attack, a TIA, or full stroke (the kind caused by a clot). And finally, aspirin is now widely 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 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.)

As such, aspirin is the primary, first-choice antiplatelet drug.

Six groups

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

- People who have risk factors 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”
- People who have had angioplasty (a procedure to open blocked arteries)
- People who have had a heart attack, TIA, or stroke
- People who have peripheral artery disease or poor blood circulation

Taking these one by one:

■ People who have risk factors will be evaluated for aspirin treatment. If they can tolerate it, it will be prescribed. 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 – that is, it usually appears during exercise 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 very likely to be taking other medicines as well, but only rarely would they be prescribed another or second antiplatelet drug; aspirin will be 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 are just sitting around (as opposed to exerting themselves), they will have progressed to what doctors call “unstable angina.”

People with unstable angina are at much greater risk of heart attack. Indeed, unstable angina can mean that a heart attack is imminent because of 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, if you have unstable angina and acute coronary syndrome, your treatment is more complicated.

Specifically, your doctor may recommend an immediate diagnostic procedure to locate artery blockages and possibly treat them. This procedure is known as angiography. A doctor threads a thin, flexible tube into a blood vessel in your groin, and then snakes it up to your heart to visualize the coronary arteries and locate 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 put in place at that spot a tiny wire-mesh device, called a stent, to prop open the artery.

Alternatively, if a lot of blockages are found, and they are severe, your doctor may recommend coronary artery bypass surgery.

People with unstable angina and/or acute coronary syndrome will be assessed for aspirin treatment. Prior to hospitalization, they may only be prescribed aspirin. But once hospitalized or treated in an emergency room (and after that), they will almost always get other medicines, including a second antiplatelet drug.

■ Patients who have coronary angioplasty are also commonly prescribed antiplatelet drugs.

Aspirin Use and Your Heart Risk

Aspirin is the most widely used antiplatelet drug, and has been quite thoroughly studied. When taken by people who have already had a heart attack or stroke, aspirin lowers the risk of a repeat attack or stroke by about a third. 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 recommend a daily aspirin pill (81mg to 325mg) for anyone who's 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 have not had a heart attack or stroke, but are considered to be at high risk of those dangerous medical events. This mostly involves people who have high blood pressure, high cholesterol, diabetes, or who smoke or don't exercise at all, and/or who are overweight. Many doctors also include in this at-risk group all men aged 55 or over, women who have gone through menopause, and anyone who has a family history of early-age (under age 60) heart attacks and/or strokes.

Studies show aspirin can indeed lower the chances 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 must be weighed carefully against the risks it poses. Namely, aspirin can cause bleeding in the stomach even at low doses when taken everyday. It can also cause increased bleeding in menstruating women. Less commonly, it can cause bleeding in the brain, raising the risk of what is called a hemorrhagic stroke.

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

However, we advise against taking aspirin everyday on your own before (a) talking with a doctor and (b) finding out more about the risks and benefits – for example, from reliable Internet sites.

In general, people who have multiple risk factors for heart disease (for example, if they smoke, have diabetes, and do not exercise) stand to benefit more from aspirin treatment (making the downside risks worth it) than people who have no or only one risk factor.

Angioplasty and the placement of stents have become controversial. Some doctors and researchers believe that too many people are undergoing the procedure – which carries some risks and is quite expensive – instead of being first treated non-surgically with various medicines, including antiplatelet drugs.

A recent landmark study showed that, over five years, people with stable angina who took only medicines did just as well as those who had angioplasty and

stents. But people in the study whose symptoms worsened were recommended for angioplasty.

These findings have focused new attention on the importance of the antiplatelet drugs. That's because even as new research is helping doctors and patients decide who needs angioplasty and a stent and who doesn't, studies have found that people who do undergo the procedure need to take at least one and preferably two antiplatelet drugs.

In particular, the studies have found that the longer people took antiplatelet drugs after angioplasty the less likely they were to have subsequent blood clots and heart attacks. The upshot: Many who undergo angioplasty will probably benefit from taking two antiplatelet drugs for years, though exactly how long has yet to be determined.

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

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

Strokes are a bit more complex. About 85 percent of strokes are caused by blood clots – and amenable to treatment 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 a hemorrhagic stroke. In fact, they can make matters worse.

So, before you are prescribed 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 is a condition known as peripheral vascular disease and is characterized by experiencing calf pain when walking. In those without typical symptoms, this condition can be detected through a decrease in blood pressure in the leg.

Peripheral vascular disease afflicts from eight to twelve million people in the U.S., and the condition signals a higher risk for heart disease and artery blockages elsewhere in the body.

Side effects and safety

The antiplatelet drugs can cause side effects. While most are mild, the drugs can increase the risk of dangerous problems, too. Notably, all of them increase

Side Effects of the Antiplatelet Drugs

Minor; usually go away in time or are short-lived

- | | |
|------------|--------------|
| ■ Headache | ■ Flatulence |
| ■ Diarrhea | ■ Dizziness |
| ■ Nausea | |

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

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

Severe and can be 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, in which the body stops making new red blood cells

the risk of bleeding in the gastrointestinal tract and brain. (See the box above.)

Each drug has side effects specific to its chemical make-up, however. Both clopidogrel (Plavix) and ticlopidine (Ticlid), for instance, 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), the risk of TTP is very small, tenuous and could possibly be coincidental, although that has not been proved yet. Patients who take ticlopidine (Ticlid), however, have a risk for TTP much higher than those taking clopidogrel. For that reason, the FDA requires that Ticlid have what is known as a “black box warning” on its label for the risk of TTP. This warning also cautions that Ticlid has been asso-

ciated with two other blood-related conditions: neutropenia (low white blood cell count) and aplastic anemia.

The risk of TTP with ticlopidine is estimated at a non-trivial one in 2,000 to 4,000 people who take it. A similar number are at risk for aplastic anemia, a condition in which the bone marrow stops producing three types of blood cells (red, white, and platelets).

The danger of getting any of the three conditions is highest during the first three months of taking ticlopidine. During that time, patients taking the drug must have regular lab tests and physician visits. If there are signs of serious side effects, the drug is immediately stopped.

Aggrenox poses some of the same risks as aspirin (primarily, the risk of stomach bleeding), since it con-

tains aspirin. The drug has also been associated with worsening of chest pain in patients who have unstable angina or 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. These include: antacids, digoxin, theophylline, warfarin, tamoxifen, fluvas-tatin, non-steroidal anti-inflammatory drugs, and the anti-viral drug oseltamivir (Tamiflu).

The 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 summarize the evidence on the antiplatelet drugs. Although no studies have directly compared all four drugs, enough studies have compared one antiplatelet to another to allow for useful recommendations on their use in various clinical circumstances.

Surprisingly, perhaps, of the four medicines, the evidence for benefit is strongest for aspirin. That is unique for two reasons. First, the makers of brand-name drugs are usually in the best position to fund the most and largest research studies supporting the benefits of their drugs. In this case, however, early evidence in the 1960s and 1970s that aspirin had a role to play in heart disease treatment propelled a significant body of research.

Today, literally dozens of studies support the use of aspirin in patients needing a blood-thinner. And, as indicated earlier, for many people aspirin is the initial drug of choice (as long as a person is not allergic to it or suffers from stomach bleeding or ulcers).

Secondly, aspirin is one of the least expensive medicines available anywhere. Thus, no one who can potentially benefit from it has a financial barrier – a truly remarkable circumstance. In fact, as evidence of aspirin's benefits mounted over the last 20 years, many observers have noted that is ironic that one of the cheapest medicines in the world is so powerful and useful against one of the world's biggest killers – heart disease.

Aspirin is not for everyone, though, nor does it alone suit every clinical need. Indeed, as indicated in the previous section, the use of the antiplatelet drugs is complicated by the emerging common practice of prescribing a second blood thinner in addition to aspirin for many people.

To help guide your and your doctor's choice, Table 2 on page 12 presents your antiplatelet treatment choices. It compares the four drugs and chooses a "best treatment" for seven different clinical circumstances. For example, studies show that people who have severe angina and acute coronary syndrome (a reminder: such people are in imminent danger of having a heart attack) benefit more from clopidogrel (Plavix) plus aspirin than from

clopidogrel or aspirin alone. When the two were compared, clopidogrel was better than aspirin for most people with acute coronary syndrome.

For people who were actively having a heart attack, the combination of clopidogrel and aspirin has also been shown superior to either drug alone. Likewise, studies have now shown very clearly that this combination was far more effective at preventing heart attacks than aspirin alone in people who have had angioplasty and a stent implant.

As Table 2 also shows, Aggrenox has been found to be more effective than aspirin alone for people who have had a stroke.

In contrast, if you have risk factors for heart disease but have not been diagnosed with any form of heart disease, there's no good evidence that any of the newer, more expensive antiplatelet drugs are any better than aspirin alone.

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

Cost considerations are complex with this class of drugs for two reasons. First, 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.

Second, the most studied and prescribed newer antiplatelet – clopidogrel (Plavix) – is the subject of intense legal wrangling. Generic clopidogrel became available in August 2006 under unusual circumstances. The company that makes Plavix promptly sued to stop another company from distributing the

Table 1. Summary of Evidence on the Antiplatelet Drugs

Brand Name(s)	Generic Name	Effective in Preventing Heart Attacks?	Effective in Preventing Strokes?	Effective for the Treatment of Peripheral Vascular Disease?	Increased Risk of Internal Bleeding When Taken with Aspirin?
Bayer, Bufferin, Others	Aspirin	Yes	Yes	Yes	
Aggrenox	Aspirin/extended-release dipyridamole	No evidence	Yes	No evidence	Yes
Plavix	Clopidogrel	Yes	Maybe	Probably	Yes
Ticlid	Ticlopidine	Yes	Maybe	No evidence	Yes

generic version. It won, but not before the generic company sent millions of clopidogrel pills to pharmacies nationwide.

This supply of generic clopidogrel is rapidly dwindling, however, and a continued supply for 2007 is in doubt. Our source on drug prices indicates an average nationwide monthly cost for generic clopidogrel of \$134, compared to \$150 for Plavix. But a check of several U.S. based online pharmacies revealed widely varying prices for the generic – as low as \$26 up to \$112 for a month’s supply.

For the purposes of our recommendations, we assume that generic clopidogrel will become available again in the not-too-distant future, and that within six months to a year of that renewed supply, the price of clopidogrel will decline significantly as more generic companies are allowed to make and market it. In the meantime, Plavix will have to be prescribed.

Taking the evidence for 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** – if you have multiple risk factors for heart attack and stroke but have not been diagnosed with heart disease or had a heart attack TIA, or stroke

- **Aspirin** – if you have been diagnosed with heart disease and have stable angina
- **Clopidogrel (Plavix)** – if you have been diagnosed with heart disease, have stable angina and can not take aspirin
- **Aspirin + clopidogrel (Plavix)** – if you have unstable angina, acute coronary syndrome, or have had a heart attack
- **Aspirin + clopidogrel (Plavix)** – if you have undergone angioplasty and had a stent implanted in the previous year
- **Aggrenox** – if you have had a stroke or mini-stroke (transient ischemic attack, or TIA)

It’s not possible to choose a *Best Buy* drug for people with peripheral vascular disease. Very few studies have compared the drugs in the treatment of this condition. And Ticlid and Aggrenox have not been studied at all in the treatment of peripheral vascular disease.

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

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 For	Comments or Cautions
Have Heart Disease Risk Factors Only ³	Aspirin	Clopidogrel (Plavix)	Ticlopidine, Aggrenox	Don't take aspirin as a heart attack preventive without consulting your doctor.
Have Heart Disease With "Stable" Angina ⁴	Aspirin	Clopidogrel (Plavix)	Ticlopidine, Aggrenox	If chest pain worsens or starts to occur when you are not active, check with your doctor immediately.
Have Heart Disease with "Unstable" Angina, or Acute Coronary Syndrome ⁵	Aspirin + clopidogrel (Plavix) ⁶	Clopidogrel (Plavix)	Ticlopidine, Aggrenox	Aspirin + clopidogrel should not be taken by people at higher risk of stomach bleeding or ulcers.
Had a Recent Heart Attack	Aspirin + clopidogrel (Plavix) ⁶	Clopidogrel (Plavix)	Ticlopidine, Aggrenox	Caution on excess risk of stomach bleeding with combination of aspirin + clopidogrel.
Had Angioplasty and Stent Placement	Aspirin + clopidogrel (Plavix) ⁶	Clopidogrel (Plavix)	Ticlopidine, Aggrenox	Strong evidence for benefit of the combination of drugs .
Have Had a Stroke or Transient Ischemic Attack (TIA)	Aggrenox	Clopidogrel ⁷	Ticlopidine	Aspirin alone has been shown less effective than Aggrenox.
Peripheral Vascular Disease ⁸	Aspirin or Clopidogrel (Plavix)	NA	Aggrenox, Ticlopidine	Evidence gives slight advantage to clopidogrel as best initial treatment.

1. "Best Treatment" indicates best initial treatment for the majority of patients. Individual circumstances vary, however, and your doctor may 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. The major risk factors for heart disease or cerebrovascular disease are high blood pressure, high cholesterol, diabetes, and smoking. Other risk factors include being overweight, getting little or no exercise, having elevated triglyceride or C-reactive protein levels, and having a family history of early-onset heart disease.

4. Stable angina is when a person has angina symptoms – primarily chest pain – that are not severe and follow a predictable pattern.

5. Unstable angina is when a person has angina symptoms – primarily chest pain – that is more severe and frequent and occurs when they are inactive. Acute Coronary Syndrome indicates a heart attack may be imminent.

6. 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.

7. Not strong evidence for clopidogrel in preventing secondary strokes; aspirin second best choice if you can take it.

8. Peripheral vascular disease mostly involves blood clots and vein blockages in the legs. This can occur in one leg or both legs.

Age, race, gender or health status differences

Unfortunately, no studies have directly compared the effectiveness of the antiplatelet drugs in older versus younger people, in men versus women, or people of different races or ethnic backgrounds. Some studies have evaluated the drugs in people with specific health conditions – such as those with diabetes, high

blood pressure, or who have a history of previous heart surgery.

The result: all of the antiplatelet drugs helped patients with existing health conditions, but they appeared to work no better or worse than for people without these conditions.

Table 3: Costs of the Antiplatelet Drugs

Generic Name and Dose	Brand Name ¹	Frequency of Use Per Day ²	Average Monthly Cost ³
Aspirin tablet 81mg-325mg	Bayer, Bufferin, Others, and Generic	One	\$3 or less
Aspirin/dipyridamole sustained release capsule 25mg/200mg	Aggrenox	Two	\$161
Clopidogrel tablet 75mg	Plavix	One	\$150
Clopidogrel tablet 75mg ⁴	Generic	One	\$26-\$134 ⁴
Ticlopidine tablet 250mg	Ticlid	Two	\$180
Ticlopidine tablet 250mg	Generic	Two	\$66

- (1) "Generic" indicates that this drug is sold as a generic.
- (2) Frequency of use reflects usual frequency; some products may be used more or less frequently.
- (3) Prices reflect nationwide retail average for November 2006, rounded to the nearest dollar; prices are derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite.
- (4) Generic clopidogrel became available in August 2006. A legal dispute over the patent on the brand version, Plavix, now threatens to disrupt the supply of the generic in 2007. In the meantime, the generic has been available at widely varying prices. Our source on drug prices (Wolters Kluwer Health, Pharmaceutical Audit Suite) indicates an average nationwide monthly cost of \$134. We checked several U.S. based online pharmacies in March 2007, however, and found it for sale at prices as low as \$26 and up to \$112 for a month's supply.



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 your doctor and you arrive at a decision about which antiplatelet drug or dose is best 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.

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.
- 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* Antiplatelets

Our evaluation is based on an independent scientific review of the evidence on the effectiveness, safety, and adverse effects of the antiplatelet medicines. 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 antiplatelets 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 the antiplatelet drugs is available at <http://www.ohsu.edu/drugeffectiveness/reports/final.cfm>. (Note: This a long and technical document written for physicians.)

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 November 2006.

Consumers Union and *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 (and thus much less choice) in this category, and compelling evidence shows two of the more expensive medicines are beneficial in certain medical circumstances.

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 non-profit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and to create a fair marketplace. It is solely responsible for the content of this report. Its main Web sites are www.consumersunion.org and 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.

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

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