

Consumer Reports BEST BUY DRUGS™

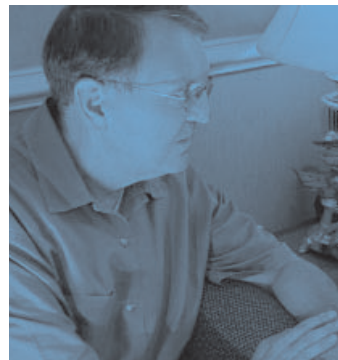
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Drugs to Treat Heartburn, Ulcers,
and Stomach Acid Reflux:

The Proton Pump Inhibitors

Comparing Effectiveness, Safety, and Price



Our Recommendations

Costs for commonly prescribed drugs to treat heartburn, ulcers, and gastroesophageal reflux disease, or GERD, vary from 79 cents a day to more than \$8.00 a day. This report compares the effectiveness, safety, and cost of five medicines in a class called proton pump inhibitors, or PPIs.

Among these are the widely advertised medicines Nexium and Prevacid, and the newly available nonprescription drug Prilosec OTC.

This report shows how you might save more than \$200 a month, or \$2,400 a year, if you have to take a PPI.

PPIs are overused and individual needs vary, so talk with your doctor about whether you need one. Your doctor may not be aware of price differences between medicines. Taking the effectiveness, safety, and cost of PPIs into account, our evaluation found that:

- If you have no health insurance or coverage for prescription drugs, omeprazole (Prilosec OTC), at a cost of around 79 cents a day, is the *Consumer Reports Best Buy Drug*. This nonprescription medicine costs one-fifth as much as the next least expensive PPI and is just as likely to relieve symptoms for most people with GERD.
- If you have drug coverage, find out if your health plan provides a discount coupon for Prilosec OTC. If not, talk with you doctor about choosing the PPI that has the lowest out-of-pocket cost under your insurance plan.

Safety Note: PPIs interact with some other medicines. If your doctor prescribes a PPI, tell him or her about any other medicines you are taking. People aged 65 and over, and people with chronic medical conditions, who take a PPI should be sure to get vaccinated against pneumonia and get a flu shot every year.

Welcome

This evaluation of a class of drugs known as “proton pump inhibitors,” or PPIs, is part of a Consumers Union and *Consumer Reports* project to help guide you to medicines that are most effective and safe, and give you the most value for your health care dollar. To learn more about the project and the other classes of drugs we examine, go to www.CRBestBuyDrugs.org.

The PPIs are used to treat heartburn, ulcers, and stomach acid reflux, also known as gastroesophageal reflux disease, or GERD. We evaluate and compare the effectiveness, safety, and cost of the five PPI medicines available in the U.S. They are:

Generic Name	Brand Name(s)
Esomeprazole	Nexium
Lansoprazole	Prevacid
Omeprazole	Prilosec and Prilosec OTC
Pantoprazole	Protonix
Rabeprazole	Aciphex

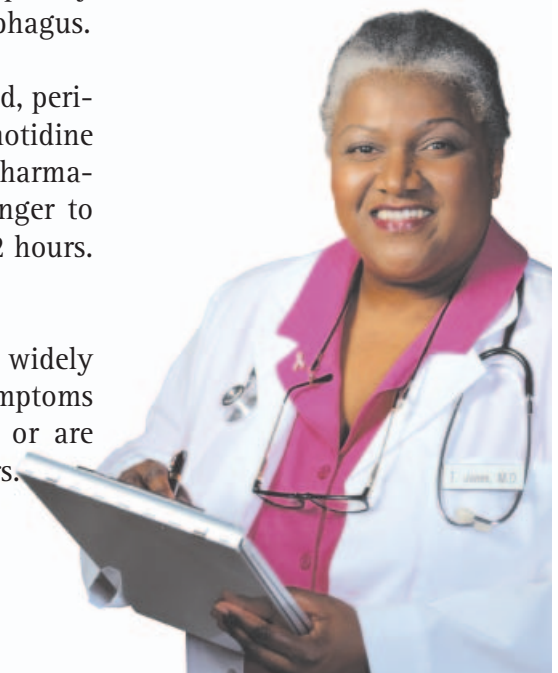
One PPI – omeprazole (Prilosec) – is now available as a generic prescription drug. A 20mg dosage form of omeprazole also is now available as a nonprescription medicine called Prilosec OTC. (OTC stands for over-the-counter.)

Other prescription and nonprescription medicines are available to treat GERD and its chief symptoms – heartburn and acid regurgitation into the esophagus. Among these are over-the-counter antacids, such as Alka Selzer, Maalox, Mylanta, Roloids, and Tums. These medicines quickly relieve heartburn caused by stomach acid backing up into the esophagus.

Another class of drugs is also available over-the-counter to treat mild, periodic heartburn. Drugs in this class include cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid), and ranitidine (Zantac). Doctors and pharmacists may refer to these drugs as the “H2 blockers.” They take longer to work, 30 minutes to an hour, but provide heartburn relief for 6 to 12 hours. Stronger doses of H2 blockers are also available by prescription.

This report evaluates only the PPIs, which have become the most widely prescribed medicines in the U.S. to treat heartburn and other symptoms associated with GERD when those symptoms persist, are severe, or are unrelieved by nonprescription medicines or prescription H2 blockers.

This report was last updated in November 2004.



What Are PPIs and Who Needs Them?

PPIs work by blocking an enzyme that makes the stomach produce more acid. This relieves heartburn, which is caused by stomach acid washing back up into the esophagus.

Almost everyone has heartburn once in a while—for example, after a heavy meal. This is not dangerous and you can usually control it by watching your diet or taking over-the-counter drugs. But some people get heartburn more often and more severely. If you have heartburn more than once a week, have frequent regurgitation of food back into your throat or mouth, or if your heartburn is not relieved by over-the-counter medicines, you may have gastroesophageal reflux disease, or GERD.

GERD can be dangerous. It can lead to esophagitis, an erosion of the lining of the esophagus. Left untreated, esophagitis can result in bleeding, scarring and narrowing of the esophagus. This can make eating and swallowing foods painful and difficult. People who have uncontrolled GERD for years also have a higher risk of cancer of the esophagus, although this cancer is rare.

Your doctor may recommend that you undergo a procedure, called endoscopy, if you have severe GERD symptoms or you have had symptoms for a long time. The procedure uses a tiny camera to look inside your esophagus.

The PPI drugs treat GERD by lowering the amount of stomach acid you produce. This relieves heartburn and helps to heal damage to the lining of the esophagus. PPIs are also used to treat peptic ulcers, which are erosions in the lining of the stomach or upper intestinal tract. These ulcers are caused primarily by a bacterial infection. PPI drug therapy alone does not eliminate the infection—you need antibiotics for that. But the PPIs help heal the ulcers by reducing stomach acid.

PPIs are very effective and safe medicines. But not everyone needs them. Some of the PPIs are widely advertised to the public and promoted to physicians—especially Nexium (esomeprazole). Many physicians believe this has led to overuse of all the PPIs.

Talk to your doctor about other medicines that may be useful for you, either before you require a PPI or in combination with a PPI. Also, talk with your doctor about the role that dietary and lifestyle changes can play in alleviating the symptoms of GERD—such as eating smaller meals, weight loss, and avoiding alcohol.

Your doctor is most likely to prescribe a PPI if your symptoms have lasted more than three months or become more severe, lifestyle modifications and other medicines have not relieved your symptoms, or endoscopy shows there is significant damage to your esophagus.



Choosing a PPI – Our *Best Buy* Picks

All the PPIs relieve heartburn and help heal the damage caused by GERD in the majority of people who take them. (See Table 1.) And they are quite similar in effectiveness and safety.

But PPIs differ greatly in cost. The average monthly cost ranges from \$24 to \$245, as you can see in Table 2.

To choose the best PPI and PPI dose, you and your doctor should consider its cost and your insurance coverage; whether you have symptoms or esophagitis that have not been relieved by other medicines; and compatibility with other medications you take.

Taking effectiveness, safety, and cost into account, our analysis concludes that over-the-counter **omeprazole (Prilosec OTC)** 20mg daily is the *Consumer Reports Best Buy Drug*. This is a proven medicine, now available without a prescription. It is as effective for most people as the more expensive prescription alternatives.

Indeed, this very same medicine was not only the most commonly prescribed PPI before its patent lapsed in late 2002, *it was the most widely prescribed drug in the country.*

Now, at an average of 79 cents a day, Prilosec OTC costs one-fifth that of the next least expensive PPI.

We understand that your health insurance status will almost certainly factor into your choice of a PPI. For most people who have no health insurance or prescription drug coverage, or who must pay a sizable portion of their drug costs out-of-pocket, **Prilosec OTC** is the clear drug of choice.

For people who have drug coverage, the decision is more complex. Insurers do not typically pay any portion of the cost for nonprescription medicines. But some insurers offer discount coupons for over-the-counter drugs like Prilosec OTC to save money and because they do not believe other prescription PPIs offer advantages for most patients. You will want first to check if your health plan offers a discount

Table 1. Comparative Effectiveness of PPIs¹

Generic Name with Dose per Day	Brand Name	Complete Symptom Relief (% of Patients)	Esophageal Healing at 8 Weeks (% of Patients)	Relapse Prevention (% of Patients)
Esomeprazole 40mg	Nexium	60-70%	92%	93%
Lansoprazole 30mg	Prevacid	60-70%	87%	NA
Omeprazole 20mg	Prilosec	60-70%	86%	86%
Pantoprazole 20mg	Protonix	60-70%	91%	86%
Rabeprazole 20mg	Aciphex	60-70%	91%	NA

(1) Effectiveness data presented for those PPI dosage strengths that have been studied and compared to date.

coupon for Prilosec OTC, and how much the coupon is good for.

If your insurance plan does *not* offer a coupon for Prilosec OTC, you could either:

- Choose the PPI that has the lowest out-of-pocket cost under your insurance plan. Generic omeprazole, for example, may be available for a co-pay of \$5 to \$10 a month.
- Choose to forgo coverage and pay for Prilosec OTC out of your own pocket.

If you are one of the 15% of people with GERD who have moderate to severe symptoms or esophagitis, you may need a higher dose PPI. If you take Prilosec OTC, you could take two 20mg tablets daily at a cost of around \$50 a month.

No matter which PPI you end up taking, if it fails to relieve your symptoms, you should discuss this with your doctor. He or she may recommend increasing your dose (if you are taking 15mg or 20mg) before switching you to another PPI.

Table 2. PPI Cost Comparison

Generic Name with Dose per Day	Brand Name ¹	Average Monthly Cost ²
Esomeprazole 20mg	Nexium	\$171
Esomeprazole 40mg	Nexium	\$165
Lansoprazole 15mg delayed release lingual tablets	Prevacid	\$133
Lansoprazole 30mg delayed release lingual tablets	Prevacid	\$126
Lansoprazole 15mg sustained release tablets	Prevacid	\$164
Lansoprazole 30mg sustained release tablets	Prevacid	\$169
Lansoprazole 30mg enteric coated capsules	Prevacid	\$159
Lansoprazole 15mg delayed release suspension packets	Prevacid	\$172
Lansoprazole 30mg delayed release suspension packets	Prevacid	\$162
Omeprazole 20mg	Prilosec OTC³	\$24
Omeprazole 10mg sustained release capsules	Prilosec	\$133
Omeprazole 20mg sustained release capsules	Prilosec	\$154
Omeprazole 40mg sustained release capsules	Prilosec	\$245
Omeprazole 10mg sustained release capsules	Generic	\$120
Omeprazole 20mg sustained release capsules	Generic	\$119
Pantoprazole 20mg delayed release tablets	Protonix	\$145
Pantoprazole 40mg delayed release tablets	Protonix	\$136
Rabeprazole 20mg	Aciphex	\$165

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

(2) Prices reflect nationwide retail average for September 2004, rounded to nearest dollar; data provided by NDCHealth, a healthcare information company.

(3) This is a nonprescription (over-the-counter) version of omeprazole available at any drug store.



The Evidence

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

How Effective Are PPIs?

The PPIs have been proven to be effective and generally safe medicines. There is no evidence that any one PPI is better than another when they are compared to each other at similar doses.

Studies have evaluated PPIs based on five criteria:

- How much they reduce stomach acid
- How well they reduce heartburn and regurgitation
- How well they heal the lining of the esophagus (a condition called esophagitis)
- How well they prevent esophagitis from recurring
- How well they heal peptic ulcers

The five PPIs have roughly the same effects on acid reduction, when given at equivalent doses. Slight differences exist, but it is not known whether they are important for the long-term impact on healing damage to the esophagus or digestive system.

PPIs reduce stomach acid better than competing classes of medicines, especially drugs known as histamine receptor antagonists or H2 blockers. This class of drugs includes such prescription and over-the-counter drugs as cimetidine (Tagamet), famotidine (Pepcid), ranitidine (Zantac), and nizatidine (Axid).

But remember, the PPIs are not intended for the *immediate* relief of heartburn. Nonprescription drugs and the H2 blockers actually do a better job at that. Rather, the main advantage of PPI therapy is reducing stomach acid more dramatically for longer periods of time.

For most people, all the PPIs are equally good at relieving symptoms after 4 to 8 weeks. Several studies show that people who take larger doses of PPIs get full relief of heartburn sooner. But no PPI relieves symptoms in all cases.

All the PPIs do a good job of healing esophagitis, the erosion or inflammation of the lining of the esophagus—leading to healing in 86% to 92% of people. Studies have found no differences in healing for these drugs at their FDA-approved starting doses: 30mg of lansoprazole (Prevacid), 20mg of omeprazole (Prilosec, Prilosec OTC, and the generic), 40mg of pantoprazole (Protonix), and 20mg of rabeprazole (Aciphex).

Esomeprazole (Nexium) at the 20mg dose is equivalent to the other PPIs. However, Nexium is almost always prescribed at a dose of 40mg. Some studies show that this dose heals esophagitis better than other PPIs given at their typical doses.

On the basis of such studies, the company that makes Nexium has claimed superiority in ads aimed at doctors and consumers. Those claims have propelled Nexium to front-runner status in PPI sales nationwide. But other recent studies show that (a) Nexium at 40mg was equivalent to Protonix at 40mg, and (b) people with GERD who did not have esophagitis fared just as well with generic Prilosec at 20mg as with Nexium at 40mg.

If you are taking any PPI and not getting the relief you need, we recommend that you talk to your doctor about taking a larger dose. An option for people without insurance or drug coverage: take two 20mg tablets of Prilosec OTC instead of one.

PPIs are effective and better than H2 blockers at preventing the return of esophagitis after it has healed.

Many people take a PPI for long periods to prevent heartburn and the damage that GERD can cause. Studies so far indicate this is safe to do. (See page 8.) However, it can be expensive. Doctors disagree about whether such long-term use is necessary, especially for people with mild symptoms that could be controlled with lifestyle changes and use of over-the-counter drugs. *Indeed, many doctors and pharmacists believe PPIs are overused to treat people who have heartburn but no sign of esophagitis.*

Finally, all the PPIs are effective—and seem to be equally so—in helping to heal stomach and peptic

ulcers, whether caused by bacterial infection or by heavy use of arthritis pain medicines.

How Safe Are PPIs?

The PPI drugs are generally safe and appear to be no different in terms of the side effects they can cause. Some 1% to 3% of people who start taking a PPI cannot tolerate it and have to stop. About 5% of people complain of headaches, usually in the first day or two of treatment. Diarrhea, the next most common side effect, occurs in about 2% to 4% of patients taking any of the PPIs except lansoprazole (Prevacid); the incidence of diarrhea is about 7% among Prevacid users.

So far, there have been few studies of the long-term use of PPIs. But those studies that have followed people taking PPIs for several years have found no difference among the drugs.

A recent study has indicated that PPIs can increase susceptibility to infections by decreasing stomach acid. Normal stomach acidity helps protect against infections by killing bacteria and viruses. Specifically, the study found that taking PPIs (as well as H2 blockers) increased the risk of pneumonia. But the increased risk was small, and this was only a single study.

Even so, we recommend that you talk to your doctor about this risk if you have asthma, lung disease, decreased immunity (due, for example, to HIV/AIDS), or are over age 65. People aged 65 and over are already advised to get vaccinated against pneumonia once and get a flu shot every year. But not all do. Taking a PPI (or H2 blocker drug) should be an even more important reason to get both vaccines.

Drug Interactions

The PPIs interact with other medicines and dietary supplements in ways that can be dangerous. Be sure to ask your doctor about this risk – even if you buy Prilosec OTC on your own.

In some cases, your doctor may recommend that you take a specific PPI because of evidence that it is less apt to interact with another drug you are taking. That's because each of the PPIs have some specific drugs with which it may interact adversely.

The main drugs to be concerned about are:

- Blood thinners, such as warfarin (Coumadin)
- Anti-anxiety drugs known as benzodiazepines (such as Tranxene and Valium)
- Antibiotics
- Phenytoin (Dilantin), used to treat epilepsy
- Disulfiram (Antabuse), used to treat alcoholism.

If you are taking one of these medicines, you should see a doctor who may want to modify the dose of your PPI or your other medicine.

Age, Race, and Gender Differences

No evidence indicates that PPIs are more or less effective or safe in people of any particular age, race, or gender. Likewise, no evidence indicates that any one PPI has an advantage over any other in any particular age or ethnic group.

However, studies indicate that about 3% of white and African-Americans, and 17–25% of Asian-Americans have less than average amounts of the enzymes that break down PPIs in the body. For such individuals, less than the usual dosage of a PPI might relieve symptoms, but the usual doses are considered to be safe. Testing to determine a person's level of this enzyme is not necessary.



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 PPI drug or dose is best for you, and which gives you the most value for your health care dollar.

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

Many people (including physicians) 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 47% of all prescriptions in the U.S. are for generics.

As you have learned in this report, one PPI – omeprazole (Prilosec and Prilosec OTC) – is available as both a prescription generic and a nonprescription drug.

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

- First, if you see several doctors, each may not be aware of medicines the others have prescribed.
- Second, since people differ in their response to medications, it is very common for doctors today to prescribe several medicines before finding one that works well or best.
- Third, many people take several prescription medications, nonprescription drugs, and dietary supplements at the same time. These can interact in ways that can either reduce the benefit you get from the drug, or be dangerous. See Table 2 on page 6 for a list of drugs that interact with PPIs in ways that should be taken into account when you are prescribed a PPI.
- And fourth, the names of prescription drugs – both generic and brand – are often hard to pronounce and remember.

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

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

How We Picked the *Best Buy* PPIs

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

A synopsis of DERP's analysis of the PPIs 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 PPIs is available at <http://www.ohsu.edu/drugeffectiveness/reports/documents/PPI%20Final%20Report%20u2.pdf>. (This a long and technical document written for physicians.)

The drug costs we cite were obtained from a health-care 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 September 2004.

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 five PPIs
- Have a safety record similar to or better than other PPIs
- Have an average price for a 30-day supply that is at least 25% lower than the most costly PPI meeting the first two criteria

The *Consumers Reports Best Buy Drugs* methodology is described in more detail in the methods section at www.CRBestBuyDrugs.org.

About Us

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