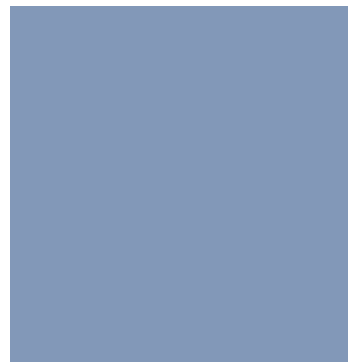
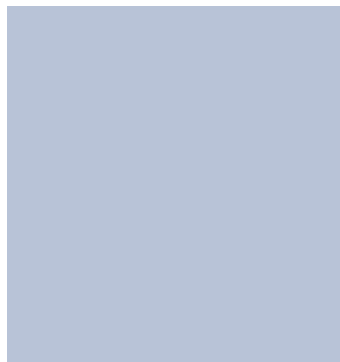
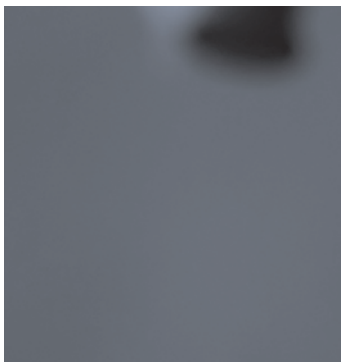
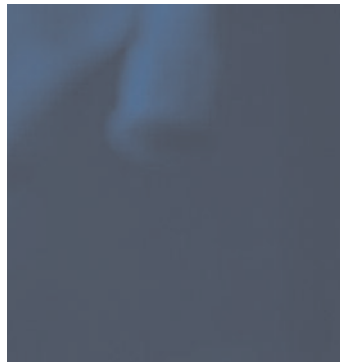


BEST BUY DRUGS

The Pegylated Interferons:

Treating Hepatitis C

Comparing Effectiveness, Safety, and Price



Our Recommendations

Pegylated interferons are used to treat hepatitis C virus infection, usually in combination with another drug called ribavirin. This combination is the treatment of choice because it's the most effective, reducing hepatitis C in the blood below detectable levels for at least six months in 55 to 60 percent of people. The likelihood of your treatment success may be higher or lower depending on the strain of virus you have. Although favorable evidence is growing, there isn't enough long-term research to know for certain if treatment decreases the risks from complications from chronic hepatitis C infection, such as liver cirrhosis, liver cancer, the need for liver transplantation, or death. In addition, combination therapy is very expensive and can cause a wide range of side effects, some serious.

More than 4 million people in the U. S. are estimated to be infected with hepatitis C, a virus that attacks the liver. It is transmitted by contact with blood and other body fluids from an infected person, most often by sharing needles used for injecting illicit drugs like heroin. It can also be transmitted sexually, by contaminated needles used for tattoos and piercings, from mother to child during birth, and by accidental needle pricks occurring in health-care workers. People who received transfusions of blood products before 1992 are also at risk.

Some people can clear the virus on their own, but most (75 to 85 percent) cannot. Hepatitis C might not cause noticeable symptoms, but if left untreated it can cause liver damage leading to liver failure and even death. Symptoms that typically occur in the late stages of the disease include jaundice, a yellowing of the skin and whites of the eyes; fatigue; and pain in the upper right side of the abdomen. The only way to know for certain you are infected is a blood test.

There are two pegylated interferons available: peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron). Neither is available as a generic, and neither has been shown to be clearly more effective or safer than the other. So the choice comes down to cost. Taking all the evidence into consideration, for people with chronic hepatitis C infection who meet the criteria for combination therapy, we recommend as our Best Buy choice:

■ PegIntron + generic ribavirin tablets

PegIntron could save you \$72 to \$820 a month over Pegasys, depending on the formulation you need. Most people will be treated for at least 24 weeks—about five and half months—and potentially up to 48 weeks, or just over 11 months. So the average savings with PegIntron could be significant, from \$403 to \$4,592 over 24 weeks to \$806 to \$9,184 over 48 weeks.

In an unusual situation, each pegylated interferon is approved to be used only in combination with a specific branded version of ribavirin (Copegus with Pegasys and Rebetol with PegIntron). But generic ribavirin tablets might be your best bet because they are significantly less expensive. A month's supply will save you \$600 to \$1,050 over Rebetol and \$1,320 to \$2,310 over Copegus, depending on the dose.

The most common side effects of combination therapy include flu-like symptoms such as muscle aches, fever, fatigue, drop in red blood cell count (anemia), depression, diarrhea, nausea, a drop in white blood cell count (neutropenia), and rashes or other skin-related problems. Life-threatening or fatal problems are rare but include suicide, relapse of drug abuse or overdose, and liver failure. If you have any signs of liver failure or a history of serious mental disorders, including major depression, bipolar disorder, or psychosis, you might not be able to take these medicines. Most doctors will not treat you with them if you drink alcohol or use illicit drugs.

Ribavirin can cause birth defects, so you should not take it if you're pregnant, planning to become pregnant, or breast-feeding, or if you're a man whose partner is trying to become pregnant. And if you are treated with ribavirin, make sure to use reliable birth control while you're taking the drug and for six months afterward.

This report was released in June 2010.

Welcome

This report compares the effectiveness, safety, and cost of the class of drugs known as pegylated interferons for treatment of chronic hepatitis C virus infection. Pegylated interferons are usually used with another antiviral drug called ribavirin.

This report is part of a Consumers Union and Consumer Reports project to help you find safe and effective medicines that give you the most value for your health-care dollar. To learn more about the project and other drugs we've evaluated, go to ConsumerReportsHealth.org/BestBuyDrugs. The information in this overview is based in part on <http://www.consumerreports.org/health/conditions-and-treatments/hepatitis-c/what-is-it.htm>.

Hepatitis C is an infectious virus that can damage your liver. The liver is an important organ because it performs more than 500 jobs, including turning your food into energy, breaking down toxins, such as alcohol and medications, and fighting infections. So if your liver is damaged, your body won't be able to function normally. If the damage is severe enough, it could jeopardize your life.

More than 4 million people in the U. S. are estimated to be infected with hepatitis C, according to the National Institute of Allergy and Infectious Diseases. About 3 million of them have chronic hepatitis C. Black people have a higher rate of infection, about six in 100. Young men are also more likely to be infected because they appear more likely to inject drugs.

Hepatitis C is typically acquired through exposure to infected body fluids, most often by injecting drugs like heroin. Infection can also be transmitted sexually, by contaminated needles used for tattoos or piercings, and by accidental needle pricks in health-care workers. Due to rigorous screening procedures, it's very rare now to get hepatitis C through exposure to blood products, although people who received such transfusions before 1992 are at risk for it.

You can't catch hepatitis by kissing, shaking hands, or sharing plates or utensils with someone who's infected. Nor can you get it if a person with the virus coughs or sneezes near you. But toothbrushes and razors used by an infected person might transmit the virus, so don't share those items.

You might not know you're infected with hepatitis C because there often aren't obvious symptoms until liver damage occurs. Symptoms can include jaundice, a yellowing of the skin and whites of the eyes; fatigue; and pain in the upper right side of your abdomen (see Table 1 on page 5). These are more likely to occur if you have been infect-

ed for a long time and your liver has become damaged. If you think you have been exposed, don't wait to see if you develop these symptoms, because they could actually be signs of liver failure and it might be too late to start treatment.

The only way to know for sure if you're infected is a blood test for the virus. People at highest risk who might want to consider testing include those who had transfusions of blood products before 1992, those who have had intimate contact with an infected person, current or former intravenous drug users, people who are HIV positive, and health-care workers who may have been exposed to body fluids of infected people, perhaps after an accidental needle prick.

Table 1. Symptoms of Liver Damage Due to Hepatitis C Infection*

- Jaundice - Your skin and white parts of your eyes turn yellow
- Tired - You feel fatigued because your liver is unable to supply your muscles with adequate energy
- Dark urine
- Pain in the upper right side of your abdomen due to swollen liver
- You don't feel hungry and you lose weight
- Nausea

Source: ConsumerReportsHealth.org

* These are more likely to occur if you have been infected for a long time. A blood test is the only way to know for sure if you're infected.

The natural course of hepatitis C infection varies by person. A small percentage of people with the virus clear it from their blood. But most people with the virus—75 to 85 percent—still have it in their body six months or longer after infection, according to the Centers for Disease Control and Prevention. This condition is called chronic hepatitis C. About 75 percent of the people with it will develop some chronic inflammation of the liver. After 20 years with hepatitis C, up to 20 percent of the people will progress to cirrhosis, a serious form of liver disease characterized by irreversible liver damage with scarring. Cirrhosis in turn can progress to end-stage liver disease or liver cancer. (This happens to 1 to 5 percent of people with chronic hepatitis C after 20 years or more.) Once cirrhosis develops, people have a much higher risk of death, and liver transplantation might be required.

Symptoms of cirrhosis include pain over the liver (which may make you feel sore over the right upper abdomen), jaundice, weak muscles, swollen ankles, and itchy skin. If you develop any of those symptoms, discuss them with your doctor.

The risk of developing chronic inflammation and scarring of the liver increases if you are older when first infected, you're a heavy drinker, and you're also infected with HIV or have other chronic liver diseases. The longer you've been infected with hepatitis C, the greater your risk of developing chronic inflammation and scarring. If you're younger when first infected, treated soon after being infected, and haven't developed significant liver damage, you're more likely to clear the virus from your body.

Genotype 1, the strain most resistant to treatment, accounts for about 75 percent of the infections in the U. S.; genotypes 2 and 3 account for about 20 percent. It's harder to clear genotype 1 hepatitis C, with only about 40 percent of the people infected with it clearing it after treatment compared with 60 to 82 percent of those infected with genotypes 2 or 3.

If you have hepatitis C, there are steps you can take to keep your liver as healthy as possible. They include avoiding alcohol, exercising, eating a healthy diet, and maintaining a healthy weight. Most doctors will not treat patients with the disease if they continue to drink alcohol or use illicit drugs. Those activities can harm the liver and cause elevations of liver function tests, which are important for determining treatment success. In addition, the continued use of illegal intravenous drugs could expose you to new hepatitis C infections.

Other measures you might want to talk to your doctor about include whether you should get immunizations recommended for people with hepatitis C, such as vaccinations against the hepatitis A and hepatitis B viruses. And many prescription and over-the-counter medications, including pain-relievers such as acetaminophen (Tylenol and generics), as well as dietary supplements, can affect the liver. So it's important to tell your doctor about any of them you're taking, and to check with him or her before you start taking anything new.

What Are Pegylated Interferons and Who Needs Them?

If you have symptoms of hepatitis C or think you might have been exposed to the virus, your doctor will probably ask if you engage in any of the following risky activities: intravenous drug use, including heroin; unprotected sex with an infected person; or sharing razors or toothbrushes with an infected person. Your doctor will also want to know if you have had transfusions of blood products before 1992, received medical treatments in a country with questionable sterilization practices, or received a tattoo or piercing.

Your doctor will also probably examine your abdomen for signs that your liver is swollen, check your skin and the whites of your eyes to see if they are yellow, and do a test to check for the presence of hepatitis C in your blood. To check whether your liver has been affected, he or she might order additional blood tests called liver enzyme tests. A liver biopsy might be done to determine whether the virus has damaged your liver.

When deciding whether you are a candidate for treatment, your doctor will assess whether you are at increased risk for developing cirrhosis based on whether blood tests, a biopsy, or imaging tests—such as a CT scan—indicate liver damage. The decision to begin treatment is a balance between the chance that your liver disease could progress, how well the treatment is expected to work, and the risk of side effects.

If your doctor thinks you might benefit from treatment, he or she will most likely recommend a pegy-

lated interferon in combination with another antiviral drug called ribavirin (Copegus, Rebetol, Ribasphere, Virazole, and generics). The goal is to eliminate hepatitis C from your body to prevent or reduce complications related to chronic liver inflammation and scarring (cirrhosis).

Interferons are proteins produced by the body to help fight infections and cancers. Artificially manufactured interferons are used to treat certain illnesses including hepatitis C. But *pegylated interferons* are a different from regular interferons—they have been modified by being linked to polyethylene glycol (PEG) molecules. This modification means the interferon is cleared more slowly from the body—making it more active for longer periods of time and therefore more effective at eliminating the virus. Studies have found that combination therapy with pegylated interferon and ribavirin results in treatment success in about 55 to 60 percent of people overall, better than a pegylated interferon alone or even treatment with an interferon and ribavirin.

There are two types of pegylated interferon available to treat hepatitis C: peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron) (see Table 2, below). Neither is available as a generic.

One advantage of pegylated interferons over nonpegylated interferons is that they can be given less frequently (once weekly vs. three times a week with nonpegylated interferon). Table 3 on page 8 is

Table 2. Pegylated Interferons for Hepatitis C Virus Infection

Generic Name	Form	Brand Name	Available as a Generic?
Peginterferon alfa-2a	Intravenous solution for subcutaneous injection	Pegasys	No
Peginterferon alfa-2b	Intravenous solution for subcutaneous injection; also available as a Redipen	PegIntron	No

an overview of the two pegylated interferons, Pegasys and PegIntron. They differ in how they are processed and cleared by the body and how they are given.

All patients receive the same dose of Pegasys (180 micrograms once weekly), but doses of PegIntron are adjusted according to body weight (1.5 micrograms per kg body weight per week).

Both pegylated interferons come as liquids in vials and are administered by injections under the skin (subcutaneous) using syringes and needles. Pegasys is available as a pre-filled, one-time use syringe. PegIntron is also available in a single-use disposable injection device called Redipen.

Each pegylated interferon is approved by the FDA to be used in combination with a specific brand of ribavirin—Copegus for Pegasys and Rebetol for PegIntron. But the two brands of ribavirin are identical pharmacologically. The brand ribavirins are also identical to generic ribavirins in terms of effectiveness and safety. Given that, we recommend using a generic ribavirin since it is significantly less expensive.

You will probably be treated for 24 or 48 weeks of combination therapy depending on the hepatitis C strain that you are infected with and your response to treatment.

Treatment is more likely to work if you have mild liver damage, or none. If you have advanced liver damage, pegylated interferon-based therapy will probably not be as effective since much of the damage is irreversible. Instead, your doctor might recommend other options, such as a liver transplant.

Other factors to be considered when deciding whether to start pegylated interferon-based therapy include the strain of hepatitis C you have and whether you're also infected with HIV or hepatitis B. If you take drugs to treat HIV infection, your doctor might adjust your medications because certain HIV drugs can harm the liver or interfere with hepatitis C treatments (see drug interactions on page 15). If you drink alcohol or use illicit drugs, your doctor will ask you to stop.

You should tell your doctor if you have a history of serious mental disorders, including major depression, bipolar disorder, or psychosis, or other medical conditions that could make it difficult to tolerate the side effects of treatment. Pegylated interferon-based therapies are less effective when doses are missed or if therapy is stopped too early, so it's important for you to discuss with your doctor anything that might prevent you from completing a full course.

Table 3. Combination Therapy with Pegylated Interferon and Ribavirin for Chronic Hepatitis C Virus Infection

Generic Name and Dose	Brand Name	Comments/Special Notes
Pegylated interferon alfa-2a - 180 mcg once weekly for up to 48 weeks	Pegasys	<ul style="list-style-type: none"> • No generic form available • Supplied in vials or in prefilled syringe • Fixed dosing • Approved for use in combination with Copegus (ribavirin)
Pegylated interferon alfa-2b - 1.0 or 1.5 mcg/kg once weekly for up to 48 weeks	PegIntron	<ul style="list-style-type: none"> • No generic form available • Supplied in vials or in Redipen delivery system • Weight-based dosing • Approved for use in combination with Rebetol (ribavirin)

Choosing a Pegylated Interferon and Our *Best Buy* Pick

Studies have found that combination therapy with a pegylated interferon is fairly effective, resulting in treatment success in 55 to 60 percent of people overall. Treatment success is defined as the “sustained virologic response”—whether the hepatitis C virus remains undetectable in a person’s blood for at least six months. In most cases, this means that the virus is highly likely to remain undetectable for at least several years, perhaps even permanently, and you are less likely to have scarring and inflammation of the liver. But the hepatitis C virus may still be in your body at very low levels, and in rare cases the virus may return to detectable levels again.

The likelihood of your treatment success may be higher or lower depending on the strain of virus you have. Although favorable evidence is growing, we don’t have enough long-term data to know for certain if treatment success with combination therapy decreases the risk of long-term complications of hepatitis C such as cirrhosis, end-stage liver disease, liver cancer, liver transplantation, or death. The first pegylated interferon was approved by the FDA in 2001, so the drugs have not been around long enough for researchers to know for sure if they lower the risk of those complications.

Large trials of combination therapy with either pegylated interferon alfa-2a or pegylated interferon alfa-2b have found that both are roughly equally effective with treatment success rates of 51 and 56 percent, respectively. This agrees with meta-analyses (evaluations that include several studies), which have found that overall, combination treatment in patients with different strains of hepatitis C are successful for an average of 55 to 60 percent of people. The largest head-to-head trial of combination therapy with the two pegylated interferons—the Individualized Dose Efficacy vs. Flat Dosing to Assess Optimal Pegylated Interferon Therapy study (IDEAL)—also found that the two regimens were equally effective for genotype 1 infection, though there were differences in how ribavirin was dosed and adjusted for side effects.

Two relatively small trials released in January 2010 found that Pegasys was more effective, with 66 to

69 percent of people overall who achieved treatment success compared with 54 percent of those taking PegIntron. But the trials had several limitations. First, they were small, each with only 320 to 431 people (about one-tenth the size of the IDEAL trial). Also, ribavirin was dosed differently in the trials, so it’s difficult to know if the differences were due to the pegylated interferons or ribavirin.

A recent meta analysis found that Pegasys was marginally better, with 47 percent of people who received the drug achieving treatment success compared with 41 percent of those who were given PegIntron. But that difference is of limited clinical significance. About 16 more people would need to be treated with Pegasys than PegIntron for one additional treatment response. The researchers concluded that despite the difference in treatment success rates, it was difficult to recommend one drug over the other because there is no long-term research showing whether this leads to a reduced risk of cirrhosis, liver cancer, and death. In addition, the evidence on side effects is sparse, so even if one drug is better at reducing the complications of hepatitis C, it’s not clear if this comes at the expense of an increased risk for adverse events.

The bottom line is that Pegasys and PegIntron perform well at achieving treatment success, and that the available evidence does not definitively show that one is clearly better than the other.

In general, combination treatment is more effective for infections involving hepatitis C genotypes 2 or 3 than for those involving genotype 1. For genotypes 2 or 3, studies have found that about 60 to 82 percent of people experience treatment success. For genotype 1, the rate is significantly lower, about 40 percent.

Because of the lower rate of treatment success with genotype 1, if you have this strain, your doctor will check to see if your hepatitis C levels have become undetectable after 24 weeks of treatment. If they have, he or she will continue the treatment for another 24 weeks. If not, treatment will be stopped because it’s unlikely that continued therapy will work. If you are infected with hepatitis C genotypes

2 or 3, you might need only 24 weeks of treatment.

Adverse events

Therapy with pegylated interferon and ribavirin can cause a variety of side effects, from minor to life-threatening and even fatal. The most common are various flu-like symptoms, such as fatigue, fever, headache, and joint and muscle pain. Most people who take pegylated interferon-based therapy will experience these. Table 4, below, lists the common side effects that you should know about if you are considering combination therapy with a pegylated interferon and ribavirin.

Other common side effects include a drop in red blood cell count (anemia), depression, diarrhea, nausea, a drop in white blood cell count (neutropenia), and rashes or other skin-related problems.

In the largest trials of combination therapy with pegylated interferon, up to half of the people experienced at least one side effect. Side effects were severe enough in 14 to 22 percent of people that they stopped treatment. In the only large trial that directly compared combination treatment with the two pegylated interferons, the rate of serious side effects was similar for both pegylated interferons, ranging from 9 to 12 percent. But in a group receiving low-dose PegIntron (1.0 mcg/kg), only 10 percent withdrew from the study due to side effects, which was lower than the 13 percent rate for both the high-dose

PegIntron regimen (1.5 mcg/kg) and the Pegasys regimen. Combination therapy with low-dose PegIntron was also associated with a lower risk of a mild drop in white blood cell counts and anemia.

Life-threatening or fatal problems are rare but they have been associated with combination therapy. These include suicide, relapse of drug abuse or overdose, bacterial infections and liver failure.

There have also been reports of dehydration and hearing impairment and loss, but it's not clear if these are due to the drugs.

Ribavirin, which is considered a potential carcinogen, comes with several special considerations. It can cause birth defects, so you should not take it if you're pregnant, planning to become pregnant, or breast-feeding, or if you're a man whose partner is trying to get pregnant. And if you are treated with ribavirin, make sure to use reliable birth control while you're taking the drug and for six months afterward. The labeling of these drugs recommends using two forms of effective contraception and taking a pregnancy test every month.

You should not take ribavirin if you have kidney disease, heart disease, or a badly damaged liver.

The pegylated interferons and ribavirin can interact with other drugs, so make sure to inform your doctor of any other medications, supplements, or

Table 4. Most Common Side Effects of Pegylated Interferon Therapy

■ Anxiety	■ Insomnia
■ Anemia (decrease in red blood cell count)	■ Irritability
■ Coughing	■ Irritation or inflammation at the injection site
■ Decreased appetite	■ Itching
■ Depression	■ Joint pain
■ Diarrhea	■ Muscle pain
■ Dizziness	■ Nausea or vomiting
■ Dry skin	■ Neutropenia (decrease in white blood cell count)
■ Fever	■ Rash
■ Hair loss	■ Shortness of breath
■ Headache	■ Weight loss

herbal preparations you are taking as well as any other medical conditions you have. See page 15 for a list of drugs that can interact with pegylated interferon-based treatment.

Our Best Buy Pick

Both Pegasys and PegIntron appear to be similarly effective in achieving a sustained, infection-free response when used in combination with ribavirin. They also have similar risks of adverse events and serious side effects, although low-dose PegIntron was associated with a slightly lower risk of withdrawal in a large study due to side effects and a drop in red and white blood counts.

So that leaves cost as the deciding factor. Neither pegylated interferon is available as a generic, and combination therapy with either is very expensive. A month's supply of Pegasys costs \$3,716. A direct comparison with PegIntron is difficult because the cost depends on how much you weigh. But as you can see in Table 5 on page 12, the monthly cost of all formulations of PegIntron, which ranges from \$2,896 to \$3,644, is less expensive than Pegasys. Overall, that's a savings of \$72 to \$820 a month depending on the dose and formulation used. Most people will be treated for at least 24 weeks (about five and a half months) and possibly for 48 weeks (a little over 11 months). So the average savings of PegIntron could be significant, ranging from \$403 to \$4,592 over 24 weeks to \$806 to \$9,184 over 48 weeks.

If you are also taking ribavirin, then generic ribavirin tablets are your best bet because they are significantly less expensive. A month's supply will save you \$600 to \$1,050 over the branded version Rebetol and \$1,320 to \$2,310 over the other brand, Copegus, depending on dose.

Therefore, for patients with chronic HCV infection who meet criteria for treatment, we recommend:

■ *PegIntron + generic ribavirin tablets*

PegIntron is similarly effective and has a similar side-effects profile as Pegasys. In addition, as we noted earlier, PegIntron is available both as an injection and in a Redipen device. If low-dose of

PegIntron is appropriate for you, it has the advantage of slightly reducing the risk of a mild drop in blood count and side effects bad enough to make you stop therapy.

If one of the two pegylated interferons causes intolerable side effects, it's likely that the other will do the same. So simply switching pegylated interferons might not be the best option. You should talk to your doctor about what to do in this situation.

Combination therapy is very expensive, so you should check with your health insurance plan before starting treatment to determine what your out-of-pocket costs will be. If you don't have health insurance look into whether you qualify for programs that will help cover some of the costs. The Partnership for Prescription Assistance (www.pparx.org) and Needy Meds (www.needymeds.com) can help you find ones you might qualify for. If you're unable to work, you might qualify for Social Security Disability Income or Supplemental Security Income benefits.

Also, shop around for the best price. The prices we quote in Table 5 are average retail costs based on a nationwide database of sales. You might be able to find lower prices online and at some large discount stores.

Table 5. Average Costs for Combination Therapy with Pegylated Interferon Plus Ribavirin¹

Generic Name and Strength	Brand Name	Typical Dosing Schedule ²	Cost Per Unit	Average Cost Per 30 Days of Use ³
Pegylated interferon alfa-2a 180 mcg	Pegasys	180 mcg once weekly	\$929	\$3,716
 Pegylated interferon alfa-2b 50 mcg	PegIntron	1.5 mcg/kg once weekly	\$724	\$2,896
 Pegylated interferon alfa-2b 80 mcg	PegIntron	1.5 mcg/kg once weekly	\$746	\$2,984
 Pegylated interferon alfa-2b 150 mcg	PegIntron	1.5 mcg/kg once weekly	\$911	\$3,644
 Pegylated interferon alfa-2b 50 mcg	PegIntron Redipen	1.5 mcg/kg once weekly	\$798	\$3,192
 Pegylated interferon alfa-2b 80 mcg	PegIntron Redipen	1.5 mcg/kg once weekly	\$809	\$3,236
 Pegylated interferon alfa-2b 120 mcg	PegIntron Redipen	1.5 mcg/kg once weekly	\$804	\$3,216
 Pegylated interferon alfa-2b 150 mcg	PegIntron Redipen	1.5 mcg/kg once weekly	\$891	\$3,564
Ribavirin Products				
Ribavirin 200 mg tablet	Copegus	800 mg - 1,400 mg daily	\$20	\$2,400 - \$4,200
 Ribavirin 200 mg tablet	Ribasphere (branded generic)	800 mg - 1,400 mg daily	\$9	\$1,080 - \$1,890
 Ribavirin 200 mg tablet	Generic	800 mg - 1,400 mg daily	\$9	\$1,080 - \$1,890
Ribavirin 200 mg capsule	Rebetol	800 mg - 1,400 mg daily	\$14	\$1,680 - \$2,940
Ribavirin 200 mg capsule	Ribasphere (branded generic)	800 mg - 1,400 mg daily	\$12	\$1,440 - \$2,520
Ribavirin 200 mg capsule	Generic	800 mg - 1,400 mg daily	\$10	\$1,200 - \$2,100

- Prices per dose and monthly costs are derived from national average retail costs for March 2009 through February 2010, rounded to the nearest dollar. Information is derived by *Consumer Reports Health Best Buy Drugs* from data provided by Wolters Kluwer Pharma Solutions. Wolters Kluwer is not involved in our analysis or recommendations.
- As recommended on labeling.
- Average monthly cost of pegylated interferons is based on one injection per week for a total of four injections per 30 days.

Evidence

This section presents more information on the effectiveness and safety of the pegylated interferons and ribavirin.

This report is based on an analysis of the scientific evidence on pegylated interferon-based treatment. More than 829 studies were identified that were published in the peer-reviewed medical literature between 1966 and 2007. From these, 166 studies were closely evaluated, ultimately including 86 in the full analysis. The 86 studies consisted of 41 reports of randomized controlled trials, five systematic reviews, and 40 uncontrolled studies that provided information on adverse events. IDEAL, the largest head-to-head trial of the pegylated interferons, which was published in 2008, was also included in our analysis. In addition, a literature search was conducted to identify relevant new trials published since 2007.

Effectiveness

Studies have found that combination therapy with pegylated interferon results in treatment success in about 55 to 60 percent of people.

The best way to evaluate the effectiveness of combination therapy with pegylated interferon and ribavirin would be to determine how much it decreases the risk of cirrhosis, end-stage liver disease, liver cancer, liver transplantation, or death. But hepatitis C infection usually does not cause these problems for years or decades, and pegylated interferon plus ribavirin has been used for only about 10 years. This means that we don't have enough long-term data to know whether pegylated interferon-based therapy reduces the risks of these complications.

So instead, most studies have evaluated treatment success based on the “sustained virologic response”—whether the hepatitis C virus remains undetectable in a person's blood for at least six months after a course of treatment. People who experience treatment success are highly likely to remain free of the virus for at least several years, perhaps even permanently. Treatment success is also associated with decreased scarring and inflammation of the liver, which might decrease the risk

of future cirrhosis and related complications (although this remains to be confirmed).

For chronic hepatitis C infection associated with liver inflammation, combination therapy with either of the pegylated interferons is more effective than pegylated interferon alone or combination therapy with a non-pegylated interferon. Systematic reviews—analyses that include the results of several different studies—have found that overall, combination treatment in patients with different strains of hepatitis C results in success in an average of 55 to 60 percent of people. Two large trials of combination therapy with pegylated interferon alfa-2a or pegylated interferon alfa-2b showed similar treatment success rates of 51 and 56 percent, respectively.

The IDEAL study is the best evidence so far about how the two pegylated interferons compare. It is the only large trial to directly compare combination therapy with the two pegylated interferons. This study involved 3,070 people with genotype 1 infections who had never received treatment. They were given Pegasys at a dose of 180 mcg/week plus ribavirin at 1,000 mg/day to 1,200 mg/day; PegIntron at a standard dose of 1.5 mcg/kg per week plus ribavirin at 800 mg/day to 1,400 mg/day; or PegIntron at a low dose of 1.0 mcg/kg per week plus ribavirin at 800 mg/day to 1,400 mg/day.

In this trial, there were no significant differences in treatment success rates between the three treatment regimens (41 vs. 40 vs. 38 percent, respectively). One factor that complicates the interpretation of the IDEAL study is that the dose of ribavirin and dose adjustments in people who experienced significant side effects were different, depending on which pegylated interferon regimen they received. However, it isn't clear if these differences affected results. In general, the treatment is more effective for infections involving hepatitis C genotypes 2 or 3 than for those involving genotype 1. For genotypes 2 or 3, studies have found that about 60 to 82 percent of the people experienced treatment success. For genotype 1, the rate is significantly lower, about 40 percent.

Safety

Combination therapy with a pegylated interferon and ribavirin can cause a variety of side effects. The most common are flu-like symptoms, but life-threatening or fatal problems, although rare, have also been associated with pegylated interferon-based treatment.

Other common side effects include anemia (a drop in red blood cell count), depression, diarrhea, nausea, neutropenia (a drop in white blood cell count), and rashes or other skin-related problems. See Table 4 on page 10 for a list of the most common side effects.

In the largest trials of combination therapy with pegylated interferon compared to combination therapy with nonpegylated interferon, 40 to 50 percent of the people experienced at least one side effect, and 14 to 22 percent stopped treatment because of a side effect. In the IDEAL study, the rate of serious side effects was similar for all three pegylated interferon therapy combination regimens, ranging from 9 to 12 percent. But the low-dose PegIntron regimen had a 10 percent rate of withdrawal due to side effects, which was lower than the 13 percent rate of both the high-dose PegIntron regimen and the Pegasys regimen. Combination therapy with low-dose PegIntron was also associated with a lower risk of mild neutropenia (15 vs. 22 vs. 27 percent) and anemia (25 vs. 31 vs. 30 percent) compared with combination therapy with high-dose pegylated interferon alfa-2b or pegylated interferon alfa-2a.

Life-threatening or fatal problems are rare. In studies, liver failure, which can be fatal, occurred in 2 percent of people. Suicide, a relapse of drug abuse or overdoses, and bacterial infections occurred in less than 1 percent of people. Other psychiatric reactions include depression and homicidal ideation. The pegylated interferons should be used with extreme caution by people who have suffered from depression previously. If you develop depression or thoughts of suicide while taking one of these drugs, you should discuss it with your doctor, who may reduce your dose, stop treatment, or recommend psychiatric therapy.

Pegylated interferon-based therapy can also cause several heart problems, including low blood pres-

sure, arrhythmias, rapid heart beat, angina, and heart attacks. If you have significant or unstable heart disease, you should not be treated with pegylated interferon-based therapy.

Pegylated interferons can cause and aggravate underactive thyroid (hypothyroidism) and overactive thyroid (hyperthyroidism) conditions.

There have also been reports of diabetes. If you develop the disease, you may need to stop treatment if it can't be controlled with medication.

People with certain blood disorders called hemoglobinopathies, which include sickle-cell anemia and thalassemia major, should not take combination therapy.

Pegylated interferons should be used with caution in people with autoimmune disorders, such as interstitial nephritis, myositis, psoriasis, rheumatoid arthritis, systemic lupus erythematosus, thrombocytopenic purpura, and thyroiditis, because the drugs might make them worse.

Pegylated interferons may also trigger or exacerbate several lung problems that can lead to serious breathing problems and even death. They include bronchiolitis obliterans, dyspnea, interstitial pneumonitis, pneumonia, pulmonary hypertension, pulmonary infiltrates, and sarcoidosis.

Pegylated interferons may trigger serious colitis, which can be fatal. Symptoms include abdominal pain, bloody diarrhea, and fever. The drug should be discontinued if you experience these symptoms.

Fatal cases of infection or inflammation of the pancreas, or pancreatitis, have been reported in people taking combination therapy. The drugs should be stopped if you develop this condition. You should let your doctor know if you experience abdominal pain that radiates to your back or feels worse after eating, or indigestion, nausea, oily or smelly stools, weight loss, or vomiting. They could be signs of pancreatitis.

Pegylated interferons can induce or worsen loss of vision and other eye problems. If you develop any eye or vision problems during treatment, you should discuss them with your doctor.

Combination therapy may also inhibit growth in children. In a study of children from 3 to 17 who were treated with PegIntron plus Rebetol, both their weight and height lagged behind the normal range for untreated children their age. Six months after treatment, their weight had rebounded to normal levels but their height had not. About 20 percent still showed signs of inhibited growth six months after treatment had stopped.

There have also been reports of dehydration, hearing impairment and loss, and strokes in people taking pegylated interferon-based therapy, but it's not clear if these problems were due to the medications.

Ribavirin

Ribavirin is considered a potential carcinogen and may also cause birth defects. So women shouldn't take the drug if they're pregnant, breast-feeding, or planning to get pregnant (To avoid birth defects, you must delay getting pregnant for at least 6 months after you have stopped taking ribavirin). Men shouldn't take ribavirin if they're with a partner who is trying to get pregnant. If you take ribavirin and are sexually active, make sure to use reliable birth control for as long as you take the drug and for six months afterward. The FDA-approved product information labels of these drugs recommend using two forms of effective contraception and taking pregnancy tests every month while under treatment and for six months afterward.

You shouldn't take ribavirin if you have kidney disease, heart disease, or a badly damaged liver. Ribavirin may also cause anemia, which has been associated with fatal and nonfatal heart attacks. If you have significant or unstable cardiac disease, you should not take this drug.

Drug Interactions

Pegasys might increase blood levels of theophylline, a drug used for treating chronic obstructive pulmonary disease and asthma. Both Pegasys and PegIntron might increase blood levels of methadone, a drug used for treating moderate to severe pain and addiction to opiate drugs, such as heroin and morphine. PegIntron might reduce the effectiveness of certain drugs, including the blood-thinner warfarin,

the anti-epileptic phenytoin, and the arrhythmia drug flecainide. So if you take any of these other drugs, make sure your doctor knows because he or she might need to adjust your dosage.

HIV drugs

Caution should be used if you are taking certain HIV drugs because several of them interact negatively with combination HCV therapy.

One study found that people taking combination HCV therapy and the HIV drug zidovudine were more likely to develop neutropenia and anemia than those not taking zidovudine. Other studies have found that ribavirin might interact with zidovudine and two other HIV drugs, lamivudine and stavudine. But there's no evidence that this results in a problem for patients.

The HIV drug didanosine (Videx and generics) should not be given with ribavirin due to reports of fatal liver failure and other serious problems in people who combined them.

Age, Race, Gender and Special Population Differences

Some studies have found that older people, black people, and heavier people are more likely to have a poorer response to combination therapy. Product labeling of the pegylated interferons suggests that caution should be used when giving these drugs to people 65 or older because flu-like adverse reactions and those involving the brain and central nervous system and heart might be more severe. In addition, adverse reactions might also be greater in people with impaired renal function. Since older people are more likely to have decreased renal function, this is another reason to be cautious about using the appropriate dose and closely monitoring their renal function.

Studies indicate that combination therapy is less effective in achieving a sustained virological response in people who weigh 165 pounds or more.

Most of the participants in a majority of the studies have been men, so there isn't enough evidence to determine if the effectiveness or safety of combination therapy varies by gender.

Talking With Your Doctor

It's important to know that the information we present here 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 hepatitis C virus treatment is best for you—if one is warranted at all—and which one 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 doctor, and that studies have found that 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) 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. 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 vs. older medicines, including generic drugs.

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

Generics are much less expensive than newer brand-name medicines but they're not lesser quality drugs. Indeed, most generics remain useful medicines even many years after first being marketed. That's why more than 60 percent of all prescriptions in the U.S. today are written 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:

- If you see several doctors, each might not be aware of medicines the others have prescribed.
- Since people differ in their response to medications, it's very common for doctors today to prescribe several medicines before finding one that works well or best.
- 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 drug or be dangerous.
- 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 it with your doctors.

And always be sure that you understand the dose of the medicine being prescribed for you and how many pills you should 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 should check to see that the dose and the number of pills per day on the container match the amount your doctor told you.

How We Picked the Best Buy Drugs

Our evaluation is primarily based on an independent scientific review of the evidence on the effectiveness, safety, and adverse effects of the pegylated interferons. A team of physicians and researchers at 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 11-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of the pegylated interferons forms the basis for this report. A consultant to *Consumer Reports Health 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 pegylated interferons is available at <http://derp.ohsu.edu/about/final-products.cfm>. (This is a long and technical document written for physicians.)

Our general advice on hepatitis C virus diagnosis and treatment is based on recent published reports and reputable online sources, including www.ConsumerReportsHealth.org.

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 between February 2009 and March 2010.

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

- Be approved by the FDA for treating infection with the hepatitis C virus.
- Be as effective or more effective than other pegylated interferons.
- Have a safety record equal to or better than other pegylated interferons.

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



About Us

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Consumer Reports Health Best Buy Drugs is a public-education project administered by Consumers Union. It is partially grant-funded. Principal current outside funding comes from the State Attorney General's Consumer and Prescriber Education Grant Program, which is funded by a multistate settlement of consumer fraud claims regarding the marketing of the prescription drug Neurontin.

The Engelberg Foundation provided a major grant to fund the creation of the project from 2004 to 2007. Additional initial funding came from the National Library of Medicine, part of the National Institutes of Health. A more detailed explanation of the project is available at ConsumerReportsHealth.org/BestBuyDrugs.

These materials are made possible by a grant from the Attorney General Consumer and Prescriber Education,

which is funded by a multistate settlement of consumer fraud claims regarding the marketing of the prescription drug Neurontin.

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Health 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*, Consumers Union and its authors, editors, publishers, licensors, 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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