

VICTRELIS (boceprevir)

What is Victrelis?

Victrelis is a hepatitis C virus (HCV) –fighting protease inhibitor that works for people with genotype 1. Victrelis blocks an important step in the hepatitis C virus life cycle. The HCV protease enzyme works like a pair of scissors; it cuts viral proteins into smaller pieces so that they can be put back together again into new virus particles (called **virions**). Hepatitis C protease inhibitors work by binding to the virus's protease enzyme—just like inserting something between scissor blades so they cannot cut.

How is it used?

Victrelis is not strong enough to work by itself; it must be used with pegylated interferon and ribavirin (PEG-IFN+RBV). These medications work together to get rid of hepatitis C by helping the immune system to get rid of HCV-infected cells, and making it difficult for the virus to reproduce.

Adding Victrelis to PEG-IFN+RBV increases cure rates among people who are being treated for the first time (called **treatment naïve**) and people who have already been treated for HCV (called **treatment experienced**).

HCV treatment begins with 4 weeks of PEG-IFN+RBV; this is called the **lead-in**. After the lead-in, Victrelis is added.

- **PEG-IFN** is injected, once weekly.
- **RBV** pills or capsules are taken twice daily, dose is according to your weight.
- **VICTRELIS** comes in daily-dose bottles. The daily dose is 12 capsules—four 200 mg capsules every 7 to 9 hours, with a snack or meal. It is important not to miss doses of Victrelis.

The length of time on treatment varies, depending on someone's past HCV treatment history, whether or not a person has cirrhosis, and how well it is working (called **response-guided therapy**), measured by how much, and when the amount of hepatitis C virus in the bloodstream (called **HCV RNA** or **viral load**) drops.

RESPONSE-GUIDED THERAPY

Response to Treatment	Combination and Treatment Duration
Treatment Naïve People	
Undetectable HCV RNA at week-8 and week-24	PEG-IFN+RBV 4-week lead-in, followed by Victrelis+PEG-IFN+RBV for another 24 weeks. Total 28 weeks.
HCV RNA <100 IU/mL at week-8, Undetectable HCV RNA at week-24	PEG-IFN+RBV 4-week lead-in, followed by Victrelis+PEG-IFN+RBV for 32 weeks, then PEG-IFN+RBV only for another 12 weeks. Total 48 weeks.
Treatment Experienced People Who are Prior Relapsers or Prior Partial Responders	
Undetectable HCV RNA at week-8 and week-24	PEG-IFN+RBV 4-week lead-in, followed by Victrelis+PEG-IFN+RBV for another 32 weeks. Total 36 weeks.
HCV RNA <100 IU/mL at week-8, Undetectable HCV RNA at week-24	PEG-IFN+RBV 4-week lead-in, followed by Victrelis+PEG-IFN+RBV for 32 weeks, then PEG-IFN+RBV only for another 12 weeks. Total 48 weeks.
Treatment Experienced People Who are Prior Null Responders	
HCV RNA <100 IU/mL at week-12, Undetectable HCV RNA at week-24	PEG-IFN+RBV 4-week lead-in, followed by Victrelis+PEG-IFN+RBV for another 44 weeks. Total 48 weeks.
People With Cirrhosis Regardless of Prior HCV Treatment History	
HCV RNA <100 IU/mL at week-12, Undetectable HCV RNA at week-24	PEG-IFN+RBV 4-week lead-in, followed by Victrelis+PEG-IFN+RBV for another 44 weeks. Total 48 weeks.

STOPPING RULES:

All people should **discontinue treatment** if they have HCV RNA ≥ 100 IU/mL at week-12, or HCV RNA > 10 -15 IU/mL at week-24.

How well does Victrelis work?

The likelihood of being cured depends on several things.

Adherence—or taking your medication as prescribed—is important, to lower the risk of drug resistance and treatment failure.

In clinical trials of Victrelis, about 65% of treatment naïve people were cured. African Americans, people with cirrhosis, and people with an IL-28B CT or TT genotype were less likely to be cured.

Re-treatment with Victrelis, PEG-IFN and RBV is more likely to work for people who **relapsed** (when HCV reappears after treatment) and **partial responders** (when HCV drops by 99% during treatment, but is still detectable at week 24) than **null responders** (when HCV RNA does not drop by 99% by week 12). Retreatment is more likely to work for partial and null responders who do not have cirrhosis.

Side effects

Make sure and talk with your health care provider about possible side effects and how they will be managed. PEG-IFN and RBV have many side effects, and Victrelis worsens some of them. Most people have at least one of these side effects, and they range from mild to very serious. Known side effects of Victrelis include a drop in neutrophils (a type of white blood cells that fight bacterial infections), anemia (a drop in red blood cells), thrombocytopenia (a drop in platelets), fatigue, nausea, vomiting, diarrhea, dysgeusia (a bad or strange taste in the mouth), headache, dizziness, jaundice, and elevated liver enzyme levels.

Does Victrelis work for people who also have HIV?

Yes, but it does not mix with many HIV drugs (see drug-drug interactions). In a clinical trial in HIV/HCV coinfecting people who had never been treated for hepatitis C, approximately 60% were cured after a 4-week PEG-IFN+RBV lead-in and 44 weeks of Victrelis plus PEG-IFN+RBV. Other clinical trials are looking at Victrelis in treatment experienced HIV/HCV coinfecting people.

Victrelis and other medications: drug-drug interactions

Victrelis should not be used with certain drugs. Talk with your health care provider and pharmacist before starting—or stopping—any medications.

For people on methadone or buprenorphine, monitoring is recommended, and a dose adjustment may be needed.

For people with HIV, Victrelis lowers levels of Norvir-boosted HIV protease inhibitors, (Reyataz, Prezista, Kaletra), and Kaletra and Prezista lower Victrelis levels. Victrelis cannot be used with non-nucleosides (Atripla, Sustiva, Viramune, Intelence, Endurant, Complera). Victrelis increases levels of some statin—or cholesterol-lowering—drugs, so it cannot be used with certain statin drugs. Victrelis should not be used with many other drugs, including certain hormonal contraceptives, anti-seizure and migraine medications, St John's Wort and some anti-tuberculosis medications. **A complete listing of drug-drug interactions is available in the prescribing information for Victrelis, and at: www.hep-druginteractions.org.**

Is there anyone who cannot use Victrelis?

People with certain serious medical conditions, women who are pregnant, nursing, or trying to become pregnant, and people taking certain medications (see Victrelis and other medications). Victrelis has not been studied in people under 18 years of age.

Access to Victrelis

Merck's patient assistance program for uninsured people (income eligibility criteria apply). Call 866-363-6379.

Co-pay assistance (Victrelis only): www.victrelis.com/boceprevir/victrelis/consumer/coupon.jsp

Access to pegylated interferon and ribavirin (for uninsured people; income eligibility criteria apply)

Peg-Intron and Rebetrol: Merck's patient assistance programs. Call 866-363-6379.

Pegasys and Copegus: Genentech's patient assistance programs. Call 888-941-3331.

What is Drug Resistance?

Each day, hepatitis C makes billions of copies of itself. Some of these copies are not identical to the original (also called **wild-type**) virus. They have changes in their genetic structure, which are called **mutations**. Mutations happen at random, but the more a virus reproduces, the more likely it is that some copies will have mutations. Mutations can make it easier—or harder—for a virus to reproduce, and can prevent drugs from being effective.

When people skip their HCV medications, the virus has an opportunity to reproduce—and some of these virions may have mutations. Once a person begins taking HCV medication again, it will kill the wild-type virus, but it may not be able to kill all the virions, because some of them may have mutations that cause drug resistance. This can lead to treatment failure.

Sometimes, the amount of drug-resistant virus shrinks over time after a person has stopped HCV treatment. But resistant virus may pop back up if the person tries the same drug, or one from the same family. No one is sure about how long HCV drug resistance lasts, or what impact it will have on a person's future treatment options.

TAG

Treatment Action Group
www.treatmentactiongroup.org/hcv