

INCIVEK (telaprevir)

What is Incivek?

Incivek is a hepatitis C virus (HCV)–fighting protease inhibitor that works for people with genotype 1. Incivek 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?

Incivek 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 Incivek 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**).

PEG-IFN, RBV and Incivek are started at the same time.

- **PEG-IFN** is injected, once weekly.
- **RBV** pills or capsules are taken twice daily, dose is according to your weight.
- **INCIVEK** comes in boxes of seven daily-dose blister packs. The daily dose is six pills—two 375 mg capsules every 7 to 9 hours—with a snack or meal that contains at least 20 grams of fat (3 table-spoons of peanut butter, 2 ounces of cheese, or a bagel and cream cheese). It is important not to miss doses of Incivek.

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 or Treatment Experienced People Who Are Prior Relapsers	
Undetectable HCV RNA at week-4 and week-12	Incivek+PEG-IFN+RBV for first 12 weeks, followed by PEG-IFN+RBV only for another 12 weeks. Total 24 weeks.
Detectable HCV RNA <1000 IU/mL at week-4 and/or week-12	Incivek+PEG-IFN+RBV for first 12 weeks, followed by PEG-IFN+RBV only for another 36 weeks. Total 48 weeks.
Treatment Experienced People Who Are Prior Partial or Null Responders	
Undetectable or HCV RNA <1000 IU/mL at week-4 and/or week-12	INCIVEK+PEG-IFN+RBV for first 12 weeks, followed by PEG-IFN+RBV only for another 36 weeks. Total 48 weeks.
People With Cirrhosis	
Undetectable or HCV RNA <1000 IU/mL at week-4 and/or week-12	INCIVEK+PEG-IFN+RBV for first 12 weeks, followed by PEG-IFN+RBV only for another 36 weeks. Total 48 weeks.

STOPPING RULES:

All people should **discontinue treatment** if they have HCV RNA >1000 IU/mL at week-4 or week-12, or if they have detectable HCV RNA (any level) at week-24.

How well does Incivek 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 Incivek, about 74% 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 Incivek, 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 Incivek 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 Incivek include a drop in white blood cells, anemia (a drop in red blood cells), thrombocytopenia (a drop in platelets), and an increase in bilirubin and uric acid levels, rash (reported as very serious in 4% of clinical trial participants), itching, hemorrhoids, anorectal itching and discomfort, nausea, vomiting, diarrhea, dysgeusia (a bad or strange taste in the mouth) and fatigue.

Does Incivek 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 74% were cured after 48 weeks of treatment (12 weeks of Incivek plus PEG-IFN+RBV, followed by 36 weeks of PEG-IFN+RBV). Other clinical trials are looking at Incivek in treatment experienced HIV/HCV coinfecting people.

Incivek and other medications: drug-drug interactions

Incivek 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, Incivek can be used with Norvir-boosted Reyataz or Isentress, plus Viread with Emtriva or Epivir. If using Atripla (or Sustiva plus Viread with Emtriva or Epivir), the dose of Incivek must be increased from 750 mg to 1125 mg. Incivek increases levels of some statin—or cholesterol-lowering—drugs, so it cannot be used with certain statin drugs. Incivek should not be used with several other drugs, including migraine medications, St John's Wort, certain sedatives, hypnotics and neuroleptics, PDE5 inhibitors (for treatment of pulmonary hypertension), and some anti-tuberculosis medications. **A complete listing of drug-drug interactions is available in Incivek's prescribing information, and at: www.hep-druginteractions.org.**

Is there anyone who cannot use Incivek?

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

Access to Incivek

Vertex's patient assistance program (for uninsured people; income eligibility criteria apply) and co-pay assistance. Call 855-837-8394 or go to www.incivek.com

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

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

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

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.

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