Telaprevir (brand name Incivo) is a new medication used to treat hepatitis C. It was approved in Europe in September 2011 for treatment of adults with genotype 1 chronic hepatitis C in combination with pegylated interferon and ribavirin.

Overall, telaprevir triple therapy cures about 75% of people who take it, but it works better for some groups than others. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

Telaprevir is no longer available in the United States. Telaprevir is still licensed in the European Union but is no longer recommended as an appropriate treatment for hepatitis C by the European Association for the Study of the Liver, owing to a higher rate of side-effects and a lower cure rate when compared to newer interferon-free treatments licensed since 2014.

How does telaprevir work?
Telaprevir is one of the new direct-acting antiviral drugs that target different steps of the hepatitis C virus (HCV) lifecycle. It is an HCV protease inhibitor, meaning it blocks the protease enzyme which the virus must use to reproduce. Telaprevir must be combined with two older drugs: pegylated interferon, which stimulates the body's own immune response against the virus, and ribavirin, which improves the effectiveness of interferon.

How is telaprevir taken?
Telaprevir is a pill that may be taken as either three tablets twice daily or two tablets three times daily. It should be taken with pegylated interferon and ribavirin pills. Telaprevir is not effective if taken alone, and this can lead to drug resistance.

All three drugs are taken together for 12 weeks. Then interferon and ribavirin alone are taken for an additional 12 or 36 weeks, depending on early response, previous treatment history and extent of liver damage. This is known as 'response-guided therapy'. Many people can be successfully treated in a total of 24 weeks – half the duration of interferon/ribavirin alone.

How effective is telaprevir?
Telaprevir works better for some people than for others. Several factors predict how well someone will respond. Telaprevir is only approved for genotype 1 hepatitis C. It is not proven effective against genotypes 2, 3 or 4. Different direct-acting antivirals work better against these other genotypes.

One of the most important factors is previous treatment history. People who are new to treatment, and those who relapsed after finishing previous treatment, have the best chance of being cured with telaprevir. Telaprevir triple therapy does not work as well for people who had only a partial response or no response to prior interferon treatment.

**Sustained responder:** a person who was successfully treated and cured of hepatitis C.

**Relaper:** a person who reached undetectable HCV viral load with previous interferon-based therapy, but relapsed, or saw the virus return, after finishing treatment.

**Partial responder:** a person who had some decrease in HCV viral load with previous treatment, but did not reach an undetectable level.

**Null responder:** a person who had little or no decrease in HCV viral load with previous treatment.
People with less advanced liver damage respond better to treatment. People with cirrhosis are less likely to be cured with telaprevir triple therapy and they may have more problems with drug side-effects.

**Telaprevir treatment response**

People who experience a rapid drop in HCV viral load soon after starting treatment are more likely to be cured. Undetectable viral load at week 4 of treatment (known as ‘rapid virological response’ or RVR) and at the end of 12 weeks of telaprevir triple therapy is a good predictor of who will be cured. This will make some patients eligible for shorter treatment. But people who do not respond well after the first 4 or 12 weeks should stop treatment, as it is unlikely to work if continued longer.

People with sustained virological response, who still have undetectable viral load at 12 or 24 weeks after finishing treatment (known as ‘SVR12’ or ‘SVR24’), are considered cured.

A clinical study called ADVANCE tested 12 weeks of telaprevir triple therapy followed by pegylated interferon/ribavirin alone for an additional 12 or 36 weeks. 75% of previously untreated people who took triple therapy were cured, compared with 44% of those who took only pegylated interferon and ribavirin.

Another study called REALIZE tested telaprevir triple therapy for 12 weeks followed by pegylated interferon/ribavirin for 36 weeks for previously treated people. Among prior relapsers, 83% of people who took telaprevir were cured, compared with 24% who took only pegylated interferon and ribavirin. But telaprevir sustained response rates were lower for previous partial responders (59%) and null responders (29%).

Telaprevir has also been tested in people with HIV and HCV co-infection, showing response rates and side-effects similar to those of people with hepatitis C alone. In one study, 74% of previously untreated patients with co-infection who took telaprevir triple therapy were cured, compared with 45% who took only pegylated interferon and ribavirin.

Telaprevir’s effectiveness in ‘real world’ use is somewhat lower than cure rates seen in clinical trials, in part because patients may be sicker or have other conditions that can make treatment more difficult.

Telaprevir triple therapy has been tested in people with advanced liver disease, including people who are awaiting or have received liver transplants. Sustained response rates are higher than those of pegylated interferon/ribavirin alone, but people with advanced liver disease often have trouble tolerating treatment side-effects.

**What are the side-effects of telaprevir?**

Telaprevir can cause some side-effects of its own, but many symptoms in people taking triple therapy are due to pegylated interferon or ribavirin. The most common side-effects of telaprevir are anaemia (low haemoglobin level), nausea, diarrhoea, skin rash, itching and anal discomfort. Skin rash is usually mild to moderate, but 5% may develop a severe rash.

Side-effects of interferon include headache, fatigue, muscle and joint aches and depression. Ribavirin also causes anaemia, which can be worse when combined with telaprevir. Ribavirin can cause birth defects and should not be used by pregnant women or their male partners.

**Does telaprevir interact with other drugs?**

Telaprevir can interact with other drugs that are processed by the same enzymes in the liver. These include some antiretroviral drugs for HIV, TB medications, heart disease drugs and psychiatric medications. Sometimes drug doses can be adjusted to overcome these interactions, but some medications should not be used together with telaprevir. Information about specific drug interactions is available online at [www.hep-druginteractions.org](http://www.hep-druginteractions.org).

**How can I get telaprevir?**

Telaprevir is available by prescription in European Union countries to treat genotype 1 hepatitis C. Ask your GP or liver specialist if telaprevir combination therapy may be a good option.

When to start treatment will depend on a number of factors, including severity of liver damage (as determined by FibroScan or a liver biopsy). People with mild liver disease may be able to wait, and new more effective and better-tolerated hepatitis C medications that can be used without interferon are coming soon. However, the decision to wait must take into account how fast your liver disease might progress – which is hard to predict – and how soon new treatments will be approved in your country.