Hepatitis C treatment factsheet

**Simeprevir (Olysio)**

Simeprevir (brand name Olysio) is a new medication used to treat hepatitis C. It was approved in Europe in May 2014 for treatment of adults with chronic hepatitis C genotypes 1 or 4.

For some people, simeprevir can shorten hepatitis C treatment time when added to pegylated interferon and ribavirin. For others, simeprevir can be used in interferon-free regimens. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

### How does simeprevir work?

Simeprevir 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. Simeprevir must be combined with other medications, which may include pegylated interferon (which stimulates the body's own immune response), ribavirin or other direct-acting antivirals that work differently.

### Who can use simeprevir?

Simeprevir is indicated for use by adults with chronic hepatitis C, meaning infection lasting more than six months. It is approved for people with HCV genotypes 1 or 4. Genotype 1 is the most common type in Europe and considered the hardest to treat.

Simeprevir is not proven effective against genotypes 2, 3, 5 or 6. Different direct-acting antivirals work better against these other genotypes.

People with HCV genotype 1a – which is harder to treat than genotype 1b – should be tested for a specific viral genetic variation before starting treatment with simeprevir. This mutation, known as Q80K, can make simeprevir less effective if it is combined with pegylated interferon and ribavirin. A Q80K test should also be considered before starting an interferon-free treatment.

Simeprevir can be used by people being treated for hepatitis C for the first time (known as 'treatment-naive') and for retreatment of people who were not cured with previous interferon-based therapy (known as ‘treatment-experienced’).

Simeprevir has been tested in people with HIV and HCV co-infection. Response rates and side-effects are similar to those of HIV-negative people, but simeprevir can interact with some HIV drugs (especially HIV protease inhibitors). People with HIV and HCV co-infection who want to take simeprevir should do so under the care of a doctor who has experience treating both infections.

Simeprevir can be used by people with all stages of compensated liver disease including cirrhosis. However, it works better for people with less advanced liver damage and people with cirrhosis may experience more serious side-effects. Simeprevir has not been tested in people with decompensated liver disease (liver failure) or people who have had liver transplants.

### How is simeprevir taken?

Simeprevir is taken as a single pill once daily with food. It is not effective if taken alone without other medications and this can lead to drug resistance.

Simeprevir may also be used with pegylated interferon where sofosbuvir is not available. People with HCV genotype 1 or 4 who have not been previously treated for hepatitis C, or who relapsed after prior interferon-based therapy, usually take simeprevir with weekly pegylated interferon injections and twice-daily ribavirin pills for 12 weeks, followed by interferon and ribavirin alone for an additional 12 weeks (total treatment duration of 24 weeks).

People who were non-responders to previous interferon-based treatment – both partial- and null-responders – usually take simeprevir with pegylated interferon and ribavirin for 12 weeks, followed by interferon and ribavirin alone for an additional 36 weeks (total treatment duration of 48 weeks).

These recommendations include people with liver cirrhosis and people with HIV and HCV co-infection. However, people who are both HIV-positive and have cirrhosis usually use the 48-week treatment duration.

Simeprevir should not be combined with the older HCV protease inhibitors boceprevir (Victrelis) or telaprevir (Incivo).

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<tr>
<th>Genotype 1</th>
<th>Combined with:</th>
<th>Length of treatment</th>
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<tr>
<td></td>
<td>Simeprevir &amp; sofosbuvir</td>
<td>12 weeks (no cirrhosis)</td>
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<td>24 weeks (with cirrhosis)</td>
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<tr>
<td>Genotype 1</td>
<td>Simeprevir &amp; sofosbuvir &amp; ribavirin</td>
<td>12 weeks (with cirrhosis)</td>
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Combination with: | Length of treatment
---|---
Genotype 4 Simeprevir & sofosbuvir | 12 weeks (no cirrhosis) 24 weeks (with cirrhosis)
Genotype 4 Simeprevir & sofosbuvir & ribavirin | 12 weeks (with cirrhosis)

### How effective is simeprevir?

Simeprevir works better for some people than for others. Several factors predict how well someone will respond to simeprevir, including extent of liver damage and previous treatment history. People with liver cirrhosis do not respond as well as those with mild or moderate liver fibrosis. People who are new to treatment have a better chance of being cured than those with little or no response to prior treatment.

However, factors that traditionally predict poor response to interferon-based therapy do not make as much difference with interferon-free treatment. These factors may be overcome by longer treatment or by adding other direct-acting antiviral drugs.

- **Sustained responder:** a person who is successfully treated and cured of hepatitis C.
- **Relapser:** 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.

### Simeprevir treatment response

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

The combination of simeprevir and sofosbuvir (Sovaldi) has been tested in several clinical trials.

The OPTIMIST studies looked at people with genotype 1 infection, with or without cirrhosis. Participants received 12 weeks of simeprevir and sofosbuvir regardless of liver disease status. Simeprevir plus sofosbuvir cured 97% of people without cirrhosis and 83% of people with cirrhosis. Treatment-experienced people with cirrhosis did less well; 73% of this group of patients was cured.

The COSMOS study looked at people with genotype 1 infection, with or without cirrhosis. Participants received 12 weeks of simeprevir and sofosbuvir with or without ribavirin for 12 or 24 weeks. 95% of people without cirrhosis were cured after 12 weeks of treatment and adding ribavirin did not improve response in this group. Twelve weeks of simeprevir and sofosbuvir with added ribavirin cured 91% of people with cirrhosis. Extending treatment to 24 weeks without ribavirin cured 100% of people with cirrhosis.

Studies of simeprevir and sofosbuvir in people with genotype 4 show 100% cure rates in people with or without cirrhosis.

Two clinical studies called QUEST-1 and QUEST-2 tested simeprevir for previously untreated people with HCV genotype 1. Participants took simeprevir or a placebo plus pegylated interferon and ribavirin for 12 weeks, followed by pegylated interferon and ribavirin alone for 12 or 36 additional weeks. The overall cure rate was 80% with simeprevir compared to 50% with the placebo.

The PROMISE study looked at people with HCV genotype 1 who relapsed after previous treatment. Using the same regimen, the overall cure rate was 79% with simeprevir compared to 37% with the placebo.

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

### What are the side-effects of simeprevir?

Simeprevir is generally well tolerated. The most common side-effects seen in people taking simeprevir with pegylated interferon and ribavirin are nausea, rash, itching, shortness of breath and increased blood bilirubin levels. Simeprevir can also cause increased sensitivity to sunlight (photosensitivity), so it is important to use sun protection.

Interferon and ribavirin can cause other side-effects including muscle and joint aches, itching, depression, anaemia (low haemoglobin level) and neutropenia (low white blood cell count). Ribavirin can also cause birth defects, so it should not be used by pregnant women or their male partners.

### Does simeprevir interact with other drugs?

Simeprevir can interact with other drugs that are processed by the same enzymes in the liver or intestines. These include some antiretroviral drugs for HIV, TB medications, antibiotics, 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 simeprevir. Information about specific drug interactions is available online at [www.hep-druginteractions.org](http://www.hep-druginteractions.org).

### How can I get simeprevir?

Simeprevir is available by prescription in several European Union countries to treat people with hepatitis C genotypes 1 or 4. Ask your GP or liver specialist if simeprevir is available in your country and if it may be a good option for you.
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 other new hepatitis C medications that can be used in interferon-free treatment 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 these new treatments will be approved in your country.