

# Hepatitis C treatment factsheet

## *Harvoni* (sofosbuvir + ledipasvir)

*Harvoni* is a new medication used to treat hepatitis C. It is a combination pill containing **sofosbuvir** (sold separately as *Sovaldi*) plus ledipasvir. It was approved in Europe in November 2014 for treatment of adults with genotype 1 or 4 chronic hepatitis C, and for some people with genotype 3.

For many people with these genotypes, *Harvoni* is an interferon-free and ribavirin-free hepatitis C treatment option. Some people with harder-to-treat disease may do better if they add ribavirin. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

### How does *Harvoni* work?

*Harvoni* contains two direct-acting antiviral drugs that target different steps of the hepatitis C virus (HCV) lifecycle. Sofosbuvir is a nucleotide analogue HCV polymerase inhibitor, meaning it blocks the polymerase enzyme which the virus must use to reproduce. Ledipasvir is an HCV NS5A replication complex inhibitor that interferes with another protein HCV uses to reproduce.

### Who can use *Harvoni*?

*Harvoni* 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, and for some people with genotype 3. Genotype 1 is the most common type in Europe.

*Harvoni* 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’).

*Harvoni* has also been tested in people with HIV and HCV co-infection. Response rates and side-effects are similar to those of HIV-negative people, and *Harvoni* can be used with most HIV medications. People with HIV and HCV co-infection who want to take *Harvoni* should do so under the care of a doctor who has experience treating both infections.

*Harvoni* can be used by people with all stages of liver disease, including compensated cirrhosis, decompensated cirrhosis (laboratory abnormalities or symptoms of poor liver function) and people who are awaiting or have received a liver transplant.

### How is *Harvoni* taken?

*Harvoni* is taken as a single pill, once daily, with or without food. The length of treatment, and whether *Harvoni* should be

taken with ribavirin, depends on HCV genotype, amount of liver damage and prior treatment history.

*Harvoni* is not approved for people with HCV genotypes 2, 5 or 6. People with genotype 2 should use sofosbuvir (*Sovaldi*) plus ribavirin, not the *Harvoni* combination pill.

Recommended uses for people with HIV and HCV co-infection are the same as for HIV-negative people.

Combination		Duration
Genotype 1, 4, 5, 6		8 weeks (no cirrhosis, no previous treatment)
		12 weeks (no cirrhosis, previously treated)
		24 weeks (no cirrhosis, previous treatment, lack of future options)
Genotype 1,4,5,6	With ribavirin	24 weeks (cirrhosis or post-transplant with cirrhosis)
		12 weeks (no cirrhosis, previous treatment or post-transplant)
Genotype 3		12 weeks (cirrhosis, including decompensated cirrhosis)
	With ribavirin	24 weeks (cirrhosis and/or previous treatment)

### How effective is *Harvoni*?

*Harvoni* works better for some people than for others. Several factors predict how well someone will respond, including HCV genotype, extent of liver damage and previous treatment history.

People with advanced liver disease may not respond as well as those with mild or moderate liver fibrosis. People who are new to treatment might have a better chance of being cured than those who did not respond to prior treatment. These factors may be overcome by longer treatment or by adding ribavirin, which helps prevent relapse.

Other factors that traditionally predict poor response to interferon-based therapy do not make as much difference with interferon-free treatment.

## Harvoni treatment response

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

The phase 3 ION studies showed that the drugs in *Harvoni*, sofosbuvir plus ledipasvir, cured 94% to 100% of previously untreated and treatment-experienced people with HCV genotype 1.

ION-1 showed that previously untreated people with or without liver cirrhosis had high cure rates with 12 weeks of treatment. ION-2, a study of previously treated people, found that 24 weeks worked better than 12 weeks for those with cirrhosis. ION-3 showed that 94% of previously untreated people without cirrhosis were cured in just 8 weeks. In all of these studies, adding ribavirin did not improve cure rates.

The ERADICATE trial found that *Harvoni* without ribavirin for 12 weeks cured HCV in 98% of previously untreated people with HIV and HCV co-infection who had HCV genotype 1 and no cirrhosis.

In the SYNERGY study, 95% of participants with HCV genotype 4 – which included previously untreated and treatment-experienced people with and without cirrhosis – were cured using *Harvoni* without ribavirin for 12 weeks.

The SOLAR-1 trial showed that *Harvoni* plus ribavirin taken for 12 or 24 weeks cured 87% to 89% of people with HCV genotype 1 or 4 and decompensated cirrhosis. The same regimen led to early sustained response ('SVR4') for more than 95% of liver transplant recipients with advanced fibrosis or compensated cirrhosis, although response rates were lower for people with decompensated liver disease.

The ELECTRON-2 study showed that *Harvoni* plus ribavirin for 12 weeks cured 100% of previously untreated people with HCV genotype 3, but the cure rate fell to 64% without ribavirin.

*Harvoni'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 Harvoni?

*Harvoni* is generally well tolerated. The most common side-effects seen in clinical trials were fatigue and headache. The drugs in *Harvoni* have not been tested in pregnant or breastfeeding women. Ribavirin can cause side-effects including anaemia. It can also cause birth defects, so it should not be used by pregnant women, women planning to conceive, or their male partners.

## Does Harvoni interact with other drugs?

The drugs in *Harvoni* can interact with certain drugs processed by a protein known as 'P-gp', including some tuberculosis (TB) medications, psychiatric drugs and cholesterol-lowering drugs. *Harvoni* should not be taken with rosuvastatin (*Crestor*) or herbal products containing St. John's wort.

*Harvoni* can raise levels of the HIV drug tenofovir (*Viread*, also in several antiretroviral coformulations), so people taking these drugs together should have their kidney function checked regularly. Information about other specific drug interactions is available online at [www.hep-druginteractions.org](http://www.hep-druginteractions.org).

## How can I get Harvoni?

*Harvoni* is available by prescription in several European Union countries to treat people with hepatitis C genotypes 1 or 4, and in some cases genotype 3. When to start treatment will depend on a number of factors, including severity of liver damage (as determined by *FibroScan* or a liver biopsy). Ask your GP or liver specialist if *Harvoni* may be a good option for you, and if it is available in your country.

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This information is intended to support, rather than replace, consultation with a healthcare professional. Talk to your doctor or another member of your healthcare team for advice tailored to your situation.

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