

Hepatitis C treatment factsheet

Sofosbuvir (*Sovaldi*)

Sofosbuvir (brand name *Sovaldi*) is a new medication used to treat hepatitis C. It was approved in Europe in January 2014 for treatment of adults with all genotypes of chronic hepatitis C.

For some people, sofosbuvir will be the first interferon-free hepatitis C treatment option. For others, sofosbuvir can greatly shorten treatment when added to pegylated interferon and ribavirin. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

How does sofosbuvir work?

Sofosbuvir is one of the new direct-acting antiviral drugs that target different steps of the hepatitis C virus (HCV) lifecycle. It is a nucleotide analogue HCV polymerase inhibitor, meaning it blocks the polymerase enzyme which the virus must use to reproduce. Sofosbuvir should 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 sofosbuvir?

Sofosbuvir is indicated for use by adults with chronic hepatitis C, meaning infection lasting more than six months. It is approved for people with HCV genotype 1, 2, 3, 4, 5 or 6. Genotype 1 is the most common type in Europe and considered the hardest to treat.

Sofosbuvir 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').

Sofosbuvir 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 sofosbuvir does not interact with HIV drugs. People with co-infection who want to take sofosbuvir should do so under the care of a doctor who has experience treating both infections.

Sofosbuvir can be used by people with all stages of liver disease including compensated and decompensated cirrhosis. However, it works better for people with less advanced liver damage. Data on safety and efficacy in decompensated cirrhosis have not yet been published. People with chronic hepatitis C who are awaiting or have received a liver transplant tolerate sofosbuvir better than older medications.

How is sofosbuvir taken?

Sofosbuvir is taken as a single pill once daily with food. It is not effective if taken alone and this can lead to drug resistance.

	Combined with:	Length of treatment
Genotype 1	Peg-interferon & ribavirin	12 weeks
	Ribavirin	24 weeks
Genotype 2	Ribavirin	12 weeks
Genotype 3	Peg-interferon & ribavirin	12 weeks
	Ribavirin	24 weeks
Genotypes 4,5,6	Peg-interferon & ribavirin	12 weeks
	Ribavirin	24 weeks

People with HCV genotype 1, 4, 5 or 6 should take sofosbuvir with weekly pegylated interferon injections and twice-daily ribavirin pills for 12 weeks. Those who cannot use interferon can take sofosbuvir plus ribavirin alone for 24 weeks.

People with HCV genotype 2 should take sofosbuvir with ribavirin alone for 12 weeks. Genotype 3 is harder to treat, so these patients should either extend sofosbuvir plus ribavirin to 24 weeks, or take sofosbuvir with both pegylated interferon and ribavirin for 12 weeks.

Recommended uses people with for HIV and HCV co-infection people are the same as for HIV-negative people. Chronic hepatitis C patients who are awaiting a liver transplant should take sofosbuvir plus ribavirin, without interferon, until the transplant takes place.

How effective is sofosbuvir?

Sofosbuvir 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 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 another direct-acting antiviral drug.

Sofosbuvir treatment response

People who experience a rapid drop in HCV viral load soon after starting treatment are more likely to be cured. People with sustained virological response, who still have undetectable viral load 12 weeks after finishing treatment (known as 'SVR12'), are considered cured.

A clinical study called NEUTRINO tested sofosbuvir plus pegylated interferon and ribavirin for 12 weeks for previously untreated people with HCV genotypes 1, 4, 5 or 6 (mostly 1). The cure rate was 91% at 12 weeks post-treatment.

Sofosbuvir has not been well studied in treatment-experienced people with genotypes 1, 4, 5 and 6. In fact, there are few data at all for genotypes 5 and 6.

The FISSION study looked at previously untreated people with HCV genotypes 2 or 3. Overall, 67% of people taking sofosbuvir plus ribavirin for 12 weeks were cured – the same as the sustained response rate for people taking pegylated interferon and ribavirin for 24 weeks. However, sofosbuvir/ribavirin cured 95% of people with genotype 2, compared with 56% of those with genotype 3. For genotype 3 patients with cirrhosis, the cure rate fell to just 34%.

The FUSION trial looked at previously treated people with genotypes 2 or 3 (mostly prior relapsers) who took sofosbuvir plus ribavirin for 12 or 16 weeks. 82% of genotype 2 patients and 30% of genotype 3 patients were cured with 12 weeks of treatment. People with genotype 3, and especially those with cirrhosis, did better with 16 weeks.

The VALENCE trial showed that 24 weeks of sofosbuvir/ribavirin works best against genotype 3, raising the cure rate to 93% for previously untreated people and 77% for those being retreated. Response rates were high even for previous non-responders and people with cirrhosis using the longer duration.

The PHOTON-1 study tested sofosbuvir plus ribavirin for people with HIV and HCV co-infection. The cure rate was about 75% for people with HCV genotype 2 or 3 treated for 12 weeks, or those with genotype 1 treated for 24 weeks.

Finally, a study of hepatitis C patients with liver cancer awaiting a liver transplant found that 62% were cured, having undetectable viral load in the new liver at 12 weeks post-transplant.

Sofosbuvir'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.

Use of sofosbuvir in combinations

Sofosbuvir is also available in the combination pills *Harvoni* (in combination with ledipasvir) and *Epclusa* (in combination with velpatasvir). See the factsheets on *Harvoni* and *Epclusa* for more information about these combinations.

Sofosbuvir can also be used in combination with daclatasvir (*Daklinza*). See the factsheet on daclatasvir (*Daklinza*) for more

information about this combination.

Sofosbuvir can also be used in combination with simeprevir (*Olysio*). See the factsheet on simeprevir (*Olysio*) for more information about this combination.

What are the side-effects of sofosbuvir?

Sofosbuvir is generally well tolerated with no known specific side-effects of its own. The most common side-effects seen in people taking sofosbuvir with ribavirin or pegylated interferon/ribavirin are fatigue, headache, nausea and insomnia.

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 sofosbuvir interact with other drugs?

Sofosbuvir can interact with certain drugs processed by a protein known as 'P-gp', including some TB medications, psychiatric drugs and herbal products containing St. John's wort. Information about specific drug interactions is available online at www.hep-druginteractions.org.

How can I get sofosbuvir?

Sofosbuvir is available by prescription in European Union countries to treat all genotypes of hepatitis C. Ask your GP or liver specialist if sofosbuvir 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 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.

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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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