

Hepatitis C treatment factsheet

***Epclusa* (sofosbuvir + velpatasvir)**

Epclusa is a new medication used to treat hepatitis C. It is a combination pill containing sofosbuvir (sold separately as *Sovaldi*) plus velpatasvir. It was approved in Europe in July 2016 for treatment of adults with all genotypes (1, 2, 3, 4, 5 and 6) of chronic hepatitis C.

Epclusa is the first pangenotypic interferon-free hepatitis C treatment regimen, meaning it works against all hepatitis C genotypes. It is more effective than the older Harvoni combination (sofosbuvir + ledipasvir) for people with genotype 3. Some people with harder-to-treat disease may do better if they take *Epclusa* with ribavirin. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

How does *Epclusa* work?

Epclusa 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. Velpatasvir is an HCV NS5A replication complex inhibitor that interferes with another protein HCV uses to reproduce.

Who can use *Epclusa*?

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

Epclusa 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 therapy (known as 'treatment experienced').

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

Epclusa 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 *Epclusa* taken?

Epclusa is taken as a single pill once daily with or without food. The length of treatment is 12 weeks for people with all HCV genotypes, with or without cirrhosis.

People with decompensated cirrhosis should add ribavirin. Ribavirin may also improve effectiveness for people with genotype 3 and compensated cirrhosis. People who previously did not respond to earlier treatment with a different NS5A inhibitor may benefit from longer treatment with *Epclusa*.

Recommended uses for people with HIV and HCV co-infection are the same as for HIV-negative people, but they should be cautious about using antiretroviral medications that can interact with the drugs in *Epclusa*.

How effective is *Epclusa*?

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

Epclusa treatment response

People with sustained virological response, who have undetectable HCV viral load 12 and 24 weeks after finishing treatment (known as 'SVR12' and 'SVR24'), are considered cured.

The phase 3 ASTRAL studies showed that the drugs in *Epclusa*, sofosbuvir plus velpatasvir, are highly effective against all genotypes of HCV.

ASTRAL-1 tested *Epclusa* without ribavirin in more than 700 previously untreated and treatment-experienced people with HCV genotypes 1, 2, 4, 5 and 6, while ASTRAL-2 focused on people with genotype 2. In both studies 99% of participants were cured.

ASTRAL-3 enrolled more than 500 people with hard-to-treat genotype 3. The cure rate was 95% for people taking *Epclusa*

for 12 weeks compared to 80% for those taking sofosbuvir plus ribavirin for 24 weeks.

The ASTRAL-4 study showed that *Epclusa* works for people with decompensated cirrhosis. Cure rates were 83% for those treated with *Epclusa* alone for 12 weeks and 94% for those who added ribavirin.

ASTRAL-5 showed that people with HIV and HCV co-infection had response rates similar to those of HIV-negative people, ranging from 92% for genotype 3 to 100% for genotypes 2 and 4.

Epclusa'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 *Epclusa*?

Epclusa is generally well-tolerated. The most common side-effects reported in clinical trials were headache, fatigue and nausea. The drugs in *Epclusa* have not been tested in pregnant or breastfeeding women, or in children and adolescents with hepatitis C. *Epclusa* has not yet been tested in people with advanced decompensated cirrhosis (Child-Pugh C) or people with severe kidney dysfunction or haemodialysis. Ribavirin can cause side-effects including anaemia. It can also cause birth defects, so it should not be used by pregnant women or their male partners.

Does *Epclusa* interact with other drugs?

The drugs in *Epclusa* can interact with other drugs that are processed by the same enzymes in the liver or intestines. This can lead to low drug levels that are less effective or high levels that can cause worse side-effects. People taking other medicines or natural remedies should consult with their doctor before starting treatment with *Epclusa*.

The drugs in *Epclusa* can interact with some TB medications, psychiatric drugs, cholesterol-lowering drugs, proton pump inhibitors, the heart medication amiodarone and herbal products containing St John's wort.

Epclusa can raise levels of the HIV drug tenofovir (*Viread*, also in several antiretroviral co-formulations), 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.

How can I get *Epclusa*?

Epclusa is approved in the European Union to treat people with hepatitis C genotypes 1 through 6. 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 *Epclusa* is available in your country and if it may be a good option for you.

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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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