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Harvoni (*ledipasvir / sofosbuvir*)

An overview of Harvoni and why it is authorised in the EU

What is Harvoni and what is it used for?

Harvoni is an antiviral medicine used to treat adults and children from 3 years of age with chronic (long-term) hepatitis C, an infectious disease of the liver caused by the hepatitis C virus.

Harvoni contains the active substances ledipasvir and sofosbuvir.

How is Harvoni used?

Harvoni can only be obtained with a prescription and treatment should be started and monitored by a doctor experienced in the management of patients with chronic hepatitis C.

Harvoni is available as tablets and as granules in sachets. The granules are suitable for children and patients who cannot take tablets and they can be sprinkled on soft food, swallowed with water or swallowed dry without chewing.

For adults the recommended dose of Harvoni is one tablet containing 90 mg ledipasvir and 400 mg sofosbuvir once a day. For children and young people aged up to 18 years the daily dose is based on their weight. There are several varieties (called genotypes) of hepatitis C virus and Harvoni is recommended for use in patients with virus of genotypes 1, 4, 5 and 6 and for some patients with genotype 3. The duration of treatment with Harvoni and whether it is used alone or in combination with another medicine called ribavirin depends on the genotype of the virus and the nature of the liver problems patients have, for example if they have liver cirrhosis (scarring) or their liver is not working properly.

For more information about using Harvoni, see the package leaflet or contact your doctor or pharmacist.

How does Harvoni work?

The active substances in Harvoni, ledipasvir and sofosbuvir, block two proteins essential for the hepatitis C virus to multiply. Sofosbuvir blocks the action of a protein called NS5B RNA-dependent RNA polymerase, while ledipasvir targets a protein called NS5A. By blocking these proteins, Harvoni stops the hepatitis C virus from multiplying and infecting new cells.

Sofosbuvir has been authorised as Sovaldi since January 2014.

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What benefits of Harvoni have been shown in studies?

Harvoni has been investigated in three main studies involving a total of around 2,000 adults infected with hepatitis C virus of genotype 1 whose liver function was normal. In all three studies, the main measure of effectiveness was the number of patients whose blood tests did not show any sign of hepatitis C virus 12 weeks after the end of treatment.

In these studies, patients were given Harvoni, with or without ribavirin, for 8, 12 or 24 weeks, depending on the characteristics of the patients. Around 94% to 99% of patients given Harvoni alone had no sign of the virus 12 weeks after treatment. Ribavirin was not needed for most patients.

The studies also found that patients who have compensated cirrhosis (when the liver is scarred but it continues to work adequately) had a higher likelihood of clearing the virus when treatment was extended to 24 weeks. Patients whose infection was resistant to other antiviral medicines could also benefit from extending treatment to 24 weeks.

Supportive data showed that Harvoni in combination with ribavirin would be of benefit for some patients with genotype 3 virus.

Harvoni was also found effective in patients infected with virus of genotype 4, 5 and 6, those with decompensated cirrhosis (when the liver is scarred and does not work adequately) and those who had received a liver transplant.

Harvoni was also investigated in children and young people aged 3 to 17 years infected with hepatitis C virus (mostly genotype 1). Results from 100 patients aged 12 to 17 years showed that 98% of them had no sign of the virus 12 weeks after the end of treatment. Similarly, there were no signs of the virus in 97% of children (33 out of 34) aged 3 to 5 years and in 99% of children (91 out of 92) aged 6 to 11 years.

What are the risks associated with Harvoni?

The most common side effects with Harvoni (which may affect more than 1 in 10 people) are tiredness and headache. Harvoni must not be used together with the cholesterol medicine rosuvastatin. It must also not be used together with the following medicines which can reduce the effects of Harvoni:

- rifampicin and rifabutin (antibiotics);
- carbamazepine, phenobarbital and phenytoin (medicines for epilepsy);
- St John's wort (a herbal preparation used to treat depression and anxiety).

For the full list of all side effects and restrictions of Harvoni, see the package leaflet.

Why is Harvoni authorised in the EU?

The European Medicines Agency decided that Harvoni's benefits are greater than its risks and it can be authorised for use in the EU.

The Agency considered that treatment with Harvoni, with or without ribavirin, is highly effective for many patients with hepatitis C virus, including those who have had a liver transplant or who have compensated or decompensated cirrhosis. The side effects of Harvoni are manageable.

What measures are being taken to ensure the safe and effective use of Harvoni?

The company that markets Harvoni will carry out a study in patients who previously have had liver cancer to evaluate the risk of liver cancer returning after treatment with direct-acting antivirals such as Harvoni. This study is being carried out in light of data suggesting that patients treated with these medicines who have had liver cancer could be at risk of their cancer returning early.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Harvoni have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Harvoni are continuously monitored. Side effects reported with Harvoni are carefully evaluated and any necessary action taken to protect patients.

Other information about Harvoni

Harvoni received a marketing authorisation valid throughout the EU on 17 November 2014.

Further information on Harvoni can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/harvoni.

This overview was last updated in 05-2020.