

Harvoni (ledipasvir + sofosbuvir)

Summary

Harvoni is a direct-acting antiviral medication used to treat hepatitis C. It is a combination of two medications, sofosbuvir and ledipasvir. These two medications are co-formulated into one tablet. Harvoni is approved in Canada for the treatment of chronic hepatitis C in people over the age of 18 years with genotype 1 through 6 of the hepatitis C virus. Recommended use depends on the genotype. Harvoni is also approved in Canada for the treatment of chronic hepatitis C in children 12 years or older with genotype 1 of the hepatitis C virus. It is taken once a day with or without food for eight, 12 or 24 weeks. Harvoni has few side effects. Side effects are generally mild and temporary; they include tiredness and headache. Direct-acting antivirals are highly effective and cure over 95% of people with hepatitis C.

What is Harvoni?

Harvoni is a direct-acting antiviral medication that is used to treat hepatitis C. It is a combination of two direct-acting antivirals: sofosbuvir, which is an NS5B (hepatitis C virus non-structural protein 5B) nucleotide polymerase inhibitor, and ledipasvir, which is an NS5A (hepatitis C virus non-structural protein 5A) inhibitor.

Harvoni is approved in Canada for the treatment of chronic hepatitis C in people over the age of 18 years with genotype 1 through 6 of the hepatitis C virus. Recommended use depends on the genotype. Harvoni is also approved in Canada for the treatment of chronic hepatitis C in children who are 12 years or older with genotype 1 of the hepatitis C virus, who either do not have cirrhosis or have compensated cirrhosis.

How does Harvoni work?

Harvoni directly blocks the ability of the hepatitis C virus to make copies of itself in the liver. Sofosbuvir interferes with the reproduction of the genetic material of the hepatitis C virus and ledipasvir works by interfering with a

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protein needed by the virus. Together, they greatly reduce and then stop the production of new copies of the hepatitis C virus. Over time, these actions eliminate the hepatitis C virus from the body.

Does Harvoni cure people of hepatitis C?

Direct-acting antivirals are highly effective and cure more than 95% of people with hepatitis C. Harvoni is one of these highly effective direct-acting antiviral medications.

A cure for hepatitis C is also known as a sustained virological response (SVR). A person is cured if the hepatitis C virus is not detected in the blood 12 weeks after the end of treatment.

If a person is cured of hepatitis C, they can get hepatitis C again if they are exposed to the hepatitis C virus.

How do people with hepatitis C use Harvoni?

Harvoni is taken as one tablet, once a day, for eight, 12 or 24 weeks. The length of treatment depends on a number of factors including the genotype of the virus, past treatment experience and the absence or presence of severe liver injury. Treatment generally lasts 12 weeks. People may be eligible for eight weeks of treatment if they have never been treated before, they have genotype 1 of the hepatitis C virus, they do not have cirrhosis and they have a hepatitis C viral load below 6 million IU/ml.

Each tablet is available as a fixed-combination tablet containing 400 mg of sofosbuvir and 90 mg of ledipasvir. Harvoni can be taken with or without food.

People with certain viral genotypes or with severe liver injury may need to take Harvoni with ribavirin. Ribavirin is another type of antiviral medication; it is not a direct-acting antiviral. Information about ribavirin is included in a separate fact sheet.

How important is it to stick to treatment?

All medications work best when they are taken exactly as prescribed and directed. People taking Harvoni should take their pills every day, as prescribed by their healthcare provider. It is very important to finish the entire course of treatment. This gives the treatment the best chance of working to cure hepatitis C.

What can be done about missed doses?

When a person taking Harvoni misses a dose and it is within 18 hours of when it should have been taken, it is important to take the missed dose immediately or as soon as possible. If it has been more than 18 hours since a dose was supposed to have been taken, that dose should be skipped and the next dose should be taken at the appropriate time. A double dose should not be taken. A person should continue their treatment until all doses have been taken.

If a person finds it difficult to stick to treatment, it is important to discuss this with their nurse or doctor. Tips for sticking to treatment can be found in CATIE's *Hepatitis C: An In-Depth Guide*.

Warnings

1. Risk of hepatitis B virus reactivation in patients co-infected with hepatitis C and hepatitis B viruses

The U.S. Food and Drug Administration (FDA) recommends that all people starting hepatitis C treatment with direct-acting antiviral medications should be tested for hepatitis B before starting treatment.

There have been a small number of reports of reactivation of hepatitis B virus infection when direct-acting antivirals like Harvoni are used to treat hepatitis C infection in people who are co-infected with hepatitis B virus. Reactivation of hepatitis B virus can, in some cases, cause serious complications. People considering the use of Harvoni should speak with their doctor or nurse about their hepatitis B virus infection status.

2. Cardiovascular effects

The manufacturer of Harvoni, Gilead Sciences, states that there have been cases of problems in some people who have taken the heart drug amiodarone and medicines containing sofosbuvir. Harvoni contains sofosbuvir. Therefore, Gilead recommends that Harvoni not be used by people who take amiodarone.

3. Breastfeeding/Chestfeeding

People with infants and who are taking Harvoni should not breastfeed or chestfeed their children. It is not known whether the medication is present in human milk.

4. People under the age of 18 years

The effectiveness of treatment with Harvoni for people aged 12 to 18 years who are infected with a genotype of the hepatitis C virus other than genotype 1 has not been determined.

The safety and effectiveness of treatment with Harvoni for children under the age of 12 years has not been determined.

The safety and effectiveness of treatment with Harvoni for people under the age of 18 years with severe renal impairment or end-stage renal disease has also not been determined.

5. Special populations

People with any of the following conditions should speak with their doctor or nurse about the most appropriate hepatitis C treatment options for them:

- pregnancy or planning a pregnancy while on treatment for hepatitis C
- liver issues other than hepatitis C
- liver transplant
- co-infection with hepatitis B
- co-infection with HIV
- rare hereditary condition of galactose (milk sugar) intolerance

Harvoni is generally safe and highly effective. Anyone who is considering treatment with Harvoni should discuss all of their medical conditions with their doctor or nurse.

Side effects

The most common side effects of Harvoni are:

- fatigue (extreme tiredness)
- headache

In most cases these side effects are mild or moderate and gradually resolve.

Drug interactions

Some prescription drugs, over-the-counter drugs, herbs, supplements and other drugs (both legal and illegal) can interfere with the absorption and/or the effectiveness of Harvoni. This is called a drug interaction.

Some drugs taken for other conditions can interact with Harvoni, increasing or decreasing the level of one or both drugs in the body. Increased levels can lead to new or more severe side effects. Decreased levels may mean that the drug won't be as effective.

It is important that people discuss all medications, supplements, herbs and other drugs (both legal and illegal) they are taking with their doctor, nurse or pharmacist. If a person has more than one doctor or pharmacist, it is possible for drug interactions to get missed. Using the same pharmacy for all prescriptions can be helpful.

This fact sheet is not comprehensive and lists only some of the potential and actual drug interactions with Harvoni. Speak with a pharmacist to find out more about drug interactions with Harvoni.

The manufacturer of Harvoni does not recommend taking Harvoni with the following medications and medicinal supplements:

- amiodarone, a medication to treat irregular heartbeat

- some anti-seizure medications, such as carbamazepine (Tegretol), phenobarbital and phenytoin (Dilantin)
- some tuberculosis medications, such as rifampin and rifapentine
- the HIV medication tipranavir (Aptivus) + ritonavir (Norvir)
- the cholesterol-lowering medication rosuvastatin (Crestor)
- any medicinal herbs, especially St. John's wort (*Hypericum perforatum*), which is an herb used to treat depression, or hyperforin or hypericin, which are active ingredients in St. John's wort

When Harvoni is taken with the following medications it could potentially cause significant drug interactions:

- antacids or buffered medications, such as Tums, milk of magnesia and calcium supplements
- medications to treat indigestion, heartburn or ulcers, such as nizatidine (Axid), famotidine (Pepcid AC, Peptic Guard), ranitidine (Zantac), esomeprazole (Nexium), lansoprazole (Prevacid), omeprazole (Losec), pantoprazole (Pantoloc), rabeprazole (Aciphex) and cimetidine (Tagamet)
- the heart drug digoxin (Lanoxin, Toloxin)

Availability

Harvoni, manufactured by Gilead Sciences, has been approved by Health Canada and is available in Canada. Pharmacists are a good source of information about public and private health insurance coverage for Harvoni.

CATIE's online module "Federal, Provincial and Territorial Drug Access Programs" also contains information about Canadian drug coverage.

Note

For recommended use of Harvoni in Canada, refer to the most recent clinical guideline on the management of hepatitis C infection in Canada.

Acknowledgement

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References

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Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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