

Harvoni (ledipasvir + sofosbuvir)

Summary

Harvoni is a medication used to treat hepatitis C. It is approved in Canada for people with genotype 1 hepatitis C virus. Harvoni is a combination of ledipasvir and sofosbuvir. These two drugs are co-formulated into one tablet. It is taken once a day with or without food. Harvoni appears to have few side effects. Common side effects are generally mild and include fatigue, headache and nausea. Hepatitis C treatment can cure a person from hepatitis C. However, a person could be infected again.

What is Harvoni?

Harvoni is a medication used to treat hepatitis C (Hep C).

How does Harvoni work?

Hep C is a disease of the liver that is caused by a virus. A virus is a very tiny germ that makes copies of itself to survive by a process called replication. The Hep C virus has at least six different strains, which are also known as genotypes.

Harvoni is a direct-acting antiviral (DAA) medication. DAAs are a group of medications that directly block the ability of the hepatitis C virus to make copies of itself.

Harvoni is a combination of two DAAs. One is sofosbuvir, which is a nucleotide polymerase inhibitor, and the other is ledipasvir, which is an NS5A inhibitor. Sofosbuvir interferes

with the reproduction of the virus's genetic material, stopping the production of new Hep C virus. Ledipasvir works by interfering with a protein needed to complete the Hep C virus life cycle in the liver cell.

Hep C treatment can cure a person from Hep C. However, a person could get infected again.

How do people use Harvoni?

Harvoni is taken as one tablet once a day. Harvoni can be taken with or without food.

Harvoni is approved in Canada for people over the age of 18 with genotype 1 hepatitis C virus.

How long is treatment?

The duration of treatment is based on past treatment experience and the absence or presence of severe liver damage.

Treatment experience	Severe liver damage (cirrhosis)	Treatment length
Never been treated (treatment naïve)	No	8* to 12 weeks
Never been treated (treatment naïve)	Yes	12 weeks
Treatment experienced (with a peg-interferon combination)	No	12 weeks
Treatment experienced (with a peg-interferon combination)	Yes	24 weeks

*People who have never been treated before who do not have cirrhosis and who have a hep C viral load below 6 million IU/mL may be eligible for eight weeks of treatment. Speak to your doctor about this.

Sticking to treatment

All medications work best when they are taken exactly as prescribed and directed. This means taking the medications in the right amount and at the right time for the entire length of time that your treatment lasts. Skipping doses or stopping treatment altogether means that the treatment may not work and the chance of being cured is lower.

With some Hep C medications, there is also a chance that the virus can become resistant to the medication if it is not taken as directed. In this case, the medication will not be effective against the virus and cannot be used to treat the infection. (See the Resistance section to learn about the potential for resistance to Harvoni.)

What can you do if you forget to take your medication?

If you miss taking a dose of Harvoni and it is within 18 hours of when you were supposed to

take it, take it as soon as possible. If it is after 18 hours from when you were supposed to take it, wait and take the next tablet at your regular time. Do not take a double dose.

If you find that you are not able to take your medication as prescribed and directed, talk to your nurse or doctor right away. You can also check out the section “Tips for staying on track with treatment” in CATIE’s *Hepatitis C: An in-depth guide* at www.catie.ca.

How likely is a cure from treatment that includes Harvoni?

Hep C treatment can cure a person from Hep C.

In late-stage clinical trials of Harvoni, participants had the following cure rates:

People with virus genotype	Cure rate
genotype 1	93% to 99%

Sometimes in real life the cure rates can be lower than in clinical trials.

A cure for Hep C is also known as a sustained virological response (SVR). This is when the Hep C virus is no longer detected in the blood 12 or 24 weeks after treatment ends.

Warnings

1. Breastfeeding/nursing

People with infants and who are taking Harvoni should not breastfeed or nurse their children.

2. Hepatitis B

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

This is because if someone has hepatitis C and hepatitis B and is not receiving treatment for hepatitis B, treatment with DAAs could reactivate hepatitis B during or after treatment. For more information about being

tested for hepatitis B, speak to your doctor or nurse.

3. Special populations

Speak to your doctor about the most appropriate treatment options if you have one or more of the following issues:

- you are pregnant
- you have liver problems other than hepatitis C
- you have severe kidney impairment or are on dialysis
- you are co-infected with hepatitis B

People who are co-infected with HIV

Clinical trials of Harvoni among people who are co-infected with HIV are ongoing. In a small clinical trial of 50 participants who were co-infected with HIV, 98% were cured. Participants were treated with Harvoni for 12 weeks.

Harvoni is a new drug and some things are unknown about its effect on people. Make sure your doctor knows about all of your medical conditions when you are discussing Harvoni as a treatment option. Harvoni has not been tested in people under the age of 18. If you are under 18, speak to your doctor about the most appropriate treatment option for you.

Side effects

The most common side effects of Harvoni are:

- fatigue
- headache
- nausea

In most cases these side effects are mild or moderate.

Drug interactions

Always consult your doctor and pharmacist about all the other prescription and non-prescription drugs you are taking, including

methadone or other opiate substitution therapies, herbs, supplements and street drugs.

Drug interactions occur when one medication affects how another is absorbed, used or flushed out of the body. Some drugs 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.

When Harvoni is taken with the following medications it could potentially cause significant drug interactions. This is not a complete list of possible drug interactions with Harvoni:

- antacids or buffered medications
- anti-seizure medication, such as carbamazepine (Tegretol), phenobarbital, oxcarbazepine (Trileptal) and phenytoin (Dilantin)
- HIV medication, such as:
 - Atripla (efavirenz + emtricitabine + tenofovir);
 - Stribild (elvitegravir + cobicistat + emtricitabine + tenofovir);
 - tenofovir (Viread and in Truvada) used together with atazanavir (Reyataz), darunavir (Prezista, Prezcofix) or Kaletra (lopinavir + ritonavir);
 - tipranavir (Aptivus) + ritonavir (Norvir)
- medication to treat indigestion, heartburn or ulcers, such as nizatidine (Axid), famotidine (Pepcid AC, Peptic Guard), ranitidine (Zantac), esomeprazole (Nexium), lansoprazole (Prevacid), omeprazole (Losec) and pantoprazole (Pantoloc)
- cholesterol-lowering medication, such as rosuvastatin (Crestor)
- some hepatitis C medications, such as simeprevir (Galexos)
- tuberculosis medication, such as rifampin

- any medicinal herbs, especially an herb used to treat depression – St. John’s wort (*Hypericum perforatum*), or hyperforin or hypericin, active ingredients in St. John’s wort

Talk to your nurse, doctor and pharmacist if you are taking any of these medicines. One way to manage drug interactions is to make sure that your doctor and pharmacist know about everything you are taking, including prescription drugs, over-the-counter drugs, street drugs, herbal medications, supplements or anything else. If you have more than one doctor or pharmacist, it is possible for drug interactions to get missed. If more than one doctor is writing prescriptions for you, let each one know about everything you are taking. If possible, use the same pharmacy for all your prescriptions.

Drug resistance

Drug resistance develops when a virus mutates, or changes, during the replication process. Some mutations of the virus may be able to resist Hep C medications. When this happens, the medication becomes less effective or stops working. Resistance to one of Harvoni’s component drugs, ledipasvir, can develop when a person does not take their medication as prescribed and directed.

In clinical trials, it was rare for the Hep C virus to develop resistance to Harvoni. However, it is still important for people taking Harvoni to take it exactly as prescribed. If you skip or miss doses, Harvoni could potentially fall to low levels in your body. This can allow the Hep C virus to mutate and become able to resist the effect of treatment.

Availability

Harvoni, manufactured by Gilead Sciences, has been approved by Health Canada and is available in Canada. Your nurse, doctor or pharmacist can tell you more about availability and coverage of Harvoni in your region.

CATIE’s online Treatment coverage in your region section of *Hepatitis C: An in-depth guide* on www.catie.ca contains information about provincial and territorial drug coverage.

Acknowledgement

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References

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