

Harvoni® (Ledipasvir/Sofosbuvir) Information Packet

Liver Disease & Hepatitis Program Providers: Brian McMahon, MD; Youssef Barbour, MD; Lisa Townshend-Bulson, FNP-C; Annette Hewitt, FNP-C; Leah Besh, PA-C; Stephen Livingston, MD

Family Medicine Provider: _____

If you are considering hepatitis C treatment, please read this treatment agreement carefully and be sure to ask any questions you may have before you begin treatment.

The FDA approved ledipasvir combined with sofosbuvir in one tablet (Harvoni®) for the treatment of hepatitis C genotypes 1, 4, 5, and 6.

PREGNANCY & BREASTFEEDING WARNING

It is not known if Harvoni® will harm an unborn or breastfeeding baby, so it is recommended that women do not get pregnant or breastfeed while taking this medicine.

PLEASE NOTE

You must let your medical, mental health, dental providers, and pharmacist(s) know that you are taking Harvoni® prior to starting any new medications. You must let Liver Clinic providers know about any new medications you are prescribed before starting them. This includes vitamins and other supplements.

If you have ever had hepatitis B infection, the virus could become active again during or after taking Harvoni®. You will have blood tests to check for hepatitis B infection before starting treatment (HBsAg, HBcAb). If you have hepatitis B or are HBcAb or HBsAg positive you will have HBV DNA levels checked before and while on treatment.

HOW THE TREATMENT PROCESS WORKS

You will have an appointment monthly while you are taking the medication.

- At each visit blood will be collected.
- A monthly pregnancy test will be done for female patients of childbearing potential.
- Random drug and alcohol tests may be requested.
- Other tests may be done during the treatment if your provider feels there is a need.

Three months after completing treatment you will have an appointment to test for cure of hepatitis C. You will then be seen yearly (corresponding to your end of treatment date) for the next 5 years. You may need to see your primary care provider during treatment if you have any other health concerns.

IF YOU HAVE ADVANCED FIBROSIS OR CIRRHOSIS

- **You should continue to have a liver ultrasound and alpha fetoprotein (AFP) cancer screening blood test every six months.**
- You will have an additional appointment in Liver Clinic 6 months after completing treatment.

Liver Clinic Provider, select the appropriate treatment regimen and reason:

_____ Harvoni® will be given for 8 weeks if you have genotype 1, do not have cirrhosis, have never been treated before, have a viral load <6 million IU/mL, are non-black, and HIV-uninfected.

_____ Harvoni® will be given for 12 weeks if:

- You have genotype 1 or 4, do not have cirrhosis or have compensated (mild) cirrhosis and have never been treated before.
- You have genotype 1, do not have cirrhosis and prior treatment with peginterferon alfa, ribavirin ± a protease inhibitor (telaprevir, boceprevir, or simeprevir) failed.
- You have genotype 4, do not have cirrhosis and prior treatment with peginterferon alfa and ribavirin failed.

_____ Harvoni® will be given for 24 weeks if you have genotype 1 or 4 hepatitis C with decompensated cirrhosis and are ribavirin ineligible.

TREATMENT MEDICATIONS AND SIDE EFFECTS

Harvoni® is a fixed-dose combination tablet containing ledipasvir 90mg and sofosbuvir 400mg. You will take Harvoni® once daily by mouth with or without food. Store the medication at room temperature. If you miss a dose, take the missed dose as soon as you remember the same day. Do not take more than 1 tablet of Harvoni® in a day. Take your next dose at your regular time the next day.

- **The most common side effects are tiredness (~16%) and headache (~14%).**

Tell your healthcare provider if you are taking any of the following medicines, as they are not recommended to be used with Harvoni® (this list is not all inclusive, medicines that are P-gp inducers are not recommended):

- Amiodarone (Cordarone®, Nexterone®, Pacerone®) [Provider note: If there is no alternative treatment option refer to full prescribing information and counsel patients about risk of symptomatic bradycardia (near-fainting, fainting, dizziness or lightheadedness, extreme tiredness, weakness, excessive tiredness, shortness of breath, chest pain, confusion, or memory problems)].
- Carbamazepine (Carbatrol®, Epitol®, Equetro®, Tegretol®)
- Oxcarbazepine (Trileptal®, Oxtellar XR®); Phenytoin (Dilantin®, Phenytek®); Phenobarbital (Luminal®); Primidone (Mysoline®)
- Rifabutin (Mycobutin®); Rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®); Rifapentine (Priftin®)
- Rosuvastatin (Crestor®)
- Simeprevir (Olysio®)
- St. John's wort (Hypericum perforatum) or a product that contains St. John's wort

- Tipranavir (Aptivus®) used in combination with ritonavir (Norvir®)
- Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate (STRIBILD®)

Tell your healthcare provider if you are taking any of the following medicines, as they require dose adjustment and/or monitoring:

- An antacid that contains aluminum or magnesium hydroxide (such as Roloids®, Maalox® and Mylanta®) must be taken 4 hours before or 4 hours after you take Harvoni®.
- Twice daily medicine for indigestion, heartburn, or stomach ulcers must be taken at the same time or 12 hours apart from Harvoni®. Famotidine (Pepcid AC®) no more than 40 mg twice daily is okay. Nizatidine (Axid®), cimetidine (Tagamet®), and ranitidine (Zantac®) have not been studied with Harvoni®.
- Once daily medications for indigestion, heartburn, or stomach ulcers must be taken at the same time as Harvoni®. Omeprazole (Prilosec®) no more than 20 mg daily is okay. Esomeprazole (Nexium®), lansoprazole (Prevacid®), rabeprazole (Aciphex®), and pantoprazole (Protonix®) have not been studied with Harvoni®.
- Atorvastatin (Lipitor®) Monitor for myopathy and rhabdomyolysis.
- Warfarin (Coumadin®) Fluctuations of INR values may occur. Frequent monitoring of INR during and post-treatment is recommended.
- Digoxin (Lanoxin®)
- Efavirenz/emtricitabine/tenofovir disoproxil fumarate (ATRIPLA®)
- Regimens containing tenofovir disoproxil fumarate (DF) (VIREAD®, TRUVADA®) without a HIV protease inhibitor/ritonavir (Norvir®) or cobicistat (Tybost®)
- Regimens containing tenofovir disoproxil fumarate (VIREAD®, TRUVADA®) with an HIV protease inhibitor/ritonavir or cobicistat (consider alternative HCV or antiviral therapy)
 - atazanavir (Reyataz®) /ritonavir (Norvir®) or cobicistat (Tybost®) + emtricitabine/tenofovir DF (TRUVADA®)
 - darunavir (Prezista®) /ritonavir (Norvir®) or cobicistat (Tybost®) + emtricitabine/tenofovir DF (TRUVADA®)
 - lopinavir/ritonavir (Kaletra®) + emtricitabine/tenofovir DF (TRUVADA®)

BENEFITS OF TREATMENT

If you have no hepatitis C in your blood 12 weeks **after** the end of treatment, you are cured. Your chance of cure depends on the hepatitis C genotype, how much virus you have in your blood at the beginning of treatment, any past treatment response, how much liver damage you have had prior to treatment, and taking the medication every day.

It is possible that you may develop some serious side effects, which will require you to stop the treatment. You may still benefit from treatment even if it does not get rid of your hepatitis C, as it may slow down the disease.

Harvoni® (Ledipasvir/Sofosbuvir) 03/2019

In Studies and Clinical Trials:

Persons with genotype 1 who were treatment-naïve (never treated before), did not have cirrhosis, and were treated with Harvoni® for 12 weeks had a 98% response (cure) rate (ION-1). In persons with cirrhosis who were treatment-naïve the response rate was 97% (ION-1).

Persons with genotype 1 with a baseline viral load of less than 6 million, who were treatment naïve, and did not have cirrhosis, the response rate was 97% (119/123) with an 8-week treatment and 96% (126/131) with 12-week treatment (ION-3).

Persons without cirrhosis in whom prior treatment with peginterferon, ribavirin and/or a protease inhibitor failed were treated for 12 and 24 weeks with Harvoni®. The response in those who took 12 weeks was 94% (33/35) (ION-2).

There are no data available on the use of Harvoni® for 24 weeks in decompensated cirrhosis. However, in one study of this regimen in persons with genotype 1 with compensated cirrhosis, who failed previous therapy with peginterferon, ribavirin, and/or a protease inhibitor, the response was 97% (Bourliere, 2015).

In persons with genotypes 4, 5 or 6 regardless of prior treatment experience or the presence or absence of compensated cirrhosis took Harvoni® for 12 weeks.

- Persons with genotype 4 had a response rate of 95%. Of these persons, 40% were treatment experienced and 43% had advanced fibrosis (Synergy Trial).
- Those with genotype 5 had a 93% (38/41) response (Study 1119).
- Those with genotype 6 had a 96% (24/25) response rate (ELECTRON-2).

To take care of your liver and prevent the spread of hepatitis C

- Do not share needles or other drug works, toothbrushes, razors, or nail clippers.
- Cover cuts to prevent blood exposure.
- Only get a tattoo if the equipment and ink used is sterile (such as at a commercial, regulated tattoo studio).
- Practice safe sex.
- Do not drink alcohol or use drugs because these hurt the liver.

WHOM TO CALL

If you have any questions about treatment, contact the Liver Disease & Hepatitis Program @ 907-729-1560 or your primary care provider.

Harvoni® Treatment Medication

You will take **Harvoni® (ledipasvir 90 mg/sofosbuvir 400 mg)**.

Take ONE tablet by mouth daily, with or without food.

The generic name for Harvoni® is ledipasvir 90mg/sofosbuvir 400mg

- An antacid that contains aluminum or magnesium hydroxide (such as Roloids®, Maalox® and Mylanta®) must be taken 4 hours before or 4 hours after you take Harvoni®.
- Twice daily medicine for indigestion, heartburn, or stomach ulcers must be taken at the same time or 12 hours apart from Harvoni®. Famotidine (Pepcid AC®) no more than 40 mg twice daily is okay. Nizatidine (Axid®), cimetidine (Tagamet®), and ranitidine (Zantac®) have not been studied with Harvoni®.
- Once daily medications for indigestion, heartburn, or stomach ulcers must be taken at the same time as Harvoni®. Omeprazole (Prilosec®) no more than 20 mg daily is okay. Esomeprazole (Nexium®), lansoprazole (Prevacid®), rabeprazole (Aciphex®), and pantoprazole (Protonix®) have not been studied with Harvoni®.
- Do not take supplements or tea containing St. John’s wort while taking Harvoni®.

Pick up refills for **Harvoni®** after monthly appointments.

For Specialty Pharmacy refills, call: _____

On these dates: _____

Call _____ to schedule your family medicine treatment appointments, or if you have any other health concerns.

Call Liver Clinic (907-729-1560) if you feel you are having any significant side effects while taking these medications, or have any other questions about treatment.

*****For any emergencies after normal business hours, please go to the Emergency Room. Make sure any healthcare provider you see knows you are on treatment. Carry a list of your medicines with you.**

For more information on managing side effects visit our website at <http://anthc.org/hep>