

Harvoni® (Ledipasvir/Sofosbuvir) & Ribavirin 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. In some circumstances, it has been found that the treatment works better or can be shortened when given with ribavirin.

PREGNANCY & BREASTFEEDING WARNING

Ribavirin can harm an unborn child or breastfeeding infant. A woman must not get pregnant and a man must not father a child while taking ribavirin and for 6 months after treatment. You must **use 2 forms of birth control** when you take ribavirin and for 6 months after your last dose.

Acceptable Birth Control Methods:

- Birth control pills or other hormone containing birth control
- Male or female condom
- Spermicides (creams, films, foams, gels, and/or suppositories)
- Diaphragm or cervical cap
- Intrauterine device (IUD), Today® vaginal sponge

Unacceptable Birth Control Methods:

- Rhythm method or withdrawal

PLEASE NOTE

You must let your medical, mental health, dental providers, and pharmacist(s) know that you are taking Harvoni® & ribavirin 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® & ribavirin. 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 2 weeks after treatment start and then monthly while you are taking the medication.

- At each visit blood will be collected.
- A pregnancy test will be done monthly for female patients of childbearing potential. If you are a woman and your treatment includes ribavirin it is recommended that you continue monthly home pregnancy testing for 6 months after treatment and notify your healthcare provider if you become pregnant. Female partners of males whose treatment includes ribavirin should do a monthly home pregnancy test during treatment and for 6 months after treatment completion and notify their health care provider if they become pregnant.
- 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 more frequently if you are having side effects or problems related to the treatment.

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:

___ Genotype 1, 4, 5, or 6 with decompensated cirrhosis, Harvoni® & low initial dose ribavirin 600mg (increased as tolerated up to weight-based dosing) will be given for 12 weeks.

___ Genotype 1, 4, 5, or 6 and are a treatment-naïve or treatment-experienced liver transplant recipient without cirrhosis or with compensated cirrhosis (Child-Pugh Class A) Harvoni® & weight-based ribavirin will be given for 12 weeks.

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[®]:

- 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®)

Ribavirin is a 200mg capsule or tablet. You will take ribavirin pills twice daily by mouth with food (dose is based on your weight). Ribavirin dose may be adjusted based on your tolerance of this medication. You should not miss/skip taking any pills. A common side effect is anemia. Anemia is a condition where the blood has a decreased number of red blood cells. This occurs more often in older persons taking ribavirin. Anemia can be serious in patients who have kidney problems. In patients who have coronary artery disease (narrowing of the blood vessels in the heart), anemia may make the problem worse, leading to chest pain or heart attack. If your provider believes you may have coronary artery disease, you will be tested for this and excluded from treatment if it is serious.

- Other common side effects include: headache, trouble sleeping, nausea, vomiting, weakness or lack of energy, shortness of breath, loss of appetite, itching, cough, muscle pain, swelling and pain in your joints (gout), depression, nervousness, and dizziness.
- Studies in animals have shown when ribavirin is given to pregnant females, death of the developing embryo or birth of deformed baby animals may result. It is expected that similar results as seen in the animal studies could occur in humans.

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.

In Studies:

Persons with genotype 1 or 4 who had decompensated cirrhosis and were treated with Harvoni® and ribavirin for 12 weeks had an 86% or better response (cure) rate (SOLAR-1).

Persons with genotype 1 or 4 who had a recurrence of hepatitis C infection after transplant had a 95% or better response rate if they had mild to advanced fibrosis or mild cirrhosis. Those with genotype 1 who had moderate cirrhosis (Child-Pugh B) had an 86% response rate. Those with genotype 1 who had advanced cirrhosis (severe/Child-Pugh C) had a 60% response rate after a 12-week treatment course of Harvoni® and ribavirin (SOLAR-1). There is no available data for persons with genotype 5 or 6.

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® & Ribavirin Treatment Medications

You will be taking:

1. Harvoni® (ledipasvir 90 mg/sofosbuvir 400 mg).

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

- 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®.

2. Ribavirin 200mg capsules

Take ___ capsules in the morning **with food** and ___ capsules in the evening **with food**. The earlier in the evening you take ribavirin, the less likely you will have sleep problems.

Pick up refills for Harvoni® & Ribavirin 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>