

## Harvoni® (Ledipasvir/Sofosbuvir) & Ribavirin Treatment Agreement

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**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 sign the form.

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.

Treatment with Harvoni® and ribavirin requires 6 scheduled visits over a 6-month period for a 12-week treatment course. If you undergo a 24-week treatment course, there are 9 scheduled visits over 9 months.

### **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 or 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

## **HOW THE TREATMENT PROCESS WORKS**

You will have blood and urine tests.

- These tests will include a pregnancy test for female patients of childbearing age. Urine pregnancy tests will be done monthly during clinic visits. 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.
- At each visit, about 2-3 tubes of blood will be collected. Other examinations and tests may be done during the treatment if your provider feels there is a need.

### **Liver Clinic Provider, select the appropriate treatment regimen:**

\_\_\_\_\_ Harvoni® & low initial dose ribavirin 600mg (increased as tolerated up to weight-based dosing) will be given for 12 weeks if you have genotype 1 hepatitis C with decompensated cirrhosis.

\_\_\_\_\_ Harvoni® & weight-based ribavirin will be given for 12 weeks if you have genotype 1 or 4 hepatitis C infection and are 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 if you have genotype 1 and do not have cirrhosis and have had previous treatment failure with sofosbuvir plus ribavirin containing regimen with or without peginterferon alfa.

Your first three visits will be at the start of treatment (week 0) and weeks 2 and 4 after you begin taking the medications. After that, the visits will be once each month until you stop taking the medications.

**You may need to come to the clinic or see your primary care provider more frequently if you are having side effects or problems related to the treatment.**

You will have a liver clinic visit 3 months after treatment completion and then yearly (corresponding to your end of treatment date) for 5 years. If you have cirrhosis you should continue to have a liver ultrasound and alpha fetoprotein (AFP) cancer screening blood test every six months and regular clinic visits.

### **TREATMENT MEDICATIONS AND SIDE EFFECTS**

**Harvoni**<sup>®</sup> is a fixed-dose combination tablet containing ledipasvir 90mg and sofosbuvir 400mg. You will take Harvoni<sup>®</sup> 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<sup>®</sup> in a day. Take your next dose at your regular time the next day.

- The most common side effects are tiredness and headache.

Tell your healthcare provider if you are taking any of the following medicines, as they are not recommended to be used with Harvoni<sup>®</sup>:

- Amiodarone (Cordarone<sup>®</sup>, Nexterone<sup>®</sup>, Pacerone<sup>®</sup>)
- Carbamazepine (Carbatrol<sup>®</sup>, Epitol<sup>®</sup>, Equetro<sup>®</sup>, Tegretol<sup>®</sup>)
- Oxycarbazepine (Trileptal<sup>®</sup>, Oxtellar XR<sup>®</sup>); Phenytoin (Dilantin<sup>®</sup>, Phenytek<sup>®</sup>); Phenobarbital (Luminal<sup>®</sup>); Primidone (Mysoline<sup>®</sup>)
- Rifabutin (Mycobutin<sup>®</sup>); Rifampin (Rifadin<sup>®</sup>, Rifamate<sup>®</sup>, Rifater<sup>®</sup>, Rimactane<sup>®</sup>); Rifapentine (Priftin<sup>®</sup>)
- Rosuvastatin (Crestor<sup>®</sup>)
- Simeprevir (Olysio<sup>®</sup>)
- St. John's wort (*Hypericum perforatum*) or a product that contains St. John's wort
- Tipranavir (Aptivus<sup>®</sup>) used in combination with ritonavir (Norvir<sup>®</sup>)
- Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate (STRIBILD<sup>®</sup>)

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<sup>®</sup>, Maalox<sup>®</sup> and Mylanta<sup>®</sup>) must be taken 4 hours before or 4 hours after you take Harvoni<sup>®</sup>.
- Twice daily medicine for indigestion, heartburn, or stomach ulcers must be taken at the same time or 12 hours apart from Harvoni<sup>®</sup>. Famotidine (Pepcid AC<sup>®</sup>) no more than 40 mg twice daily is okay. Nizatidine (Axid<sup>®</sup>), cimetidine (Tagamet<sup>®</sup>), and ranitidine (Zantac<sup>®</sup>) have not been studied with Harvoni<sup>®</sup>.
- Once daily medications for indigestion, heartburn, or stomach ulcers must be taken at the same time as Harvoni<sup>®</sup>. Omeprazole (Prilosec<sup>®</sup>) no more than 20 mg daily is okay. Esomeprazole (Nexium<sup>®</sup>), lansoprazole (Prevacid<sup>®</sup>), rabeprazole (Aciphex<sup>®</sup>), and pantoprazole (Protonix<sup>®</sup>) have not been studied with Harvoni<sup>®</sup>.
- Digoxin (Lanoxin<sup>®</sup>)
- Efavirenz/emtricitabine/tenofovir disoproxil fumarate (ATRIPLA<sup>®</sup>)
- Regimens containing tenofovir disoproxil fumarate (DF) (VIREAD<sup>®</sup>, TRUVADA<sup>®</sup>) without a HIV protease inhibitor/ritonavir (Norvir<sup>®</sup>) or cobicistat (Tybost<sup>®</sup>)
- Regimens containing tenofovir disoproxil fumarate (VIREAD<sup>®</sup>, TRUVADA<sup>®</sup>) with an HIV protease inhibitor/ritonavir or cobicistat (consider alternative HCV or antiviral therapy)
  - atazanavir (Reyataz<sup>®</sup>) /ritonavir (Norvir<sup>®</sup>) or cobicistat (Tybost<sup>®</sup>) + emtricitabine/tenofovir DF (TRUVADA<sup>®</sup>)
  - darunavir (Prezista<sup>®</sup>) /ritonavir (Norvir<sup>®</sup>) or cobicistat (Tybost<sup>®</sup>) + emtricitabine/tenofovir DF (TRUVADA<sup>®</sup>)
  - lopinavir/ritonavir (Kaletra<sup>®</sup>) + emtricitabine/tenofovir DF (TRUVADA<sup>®</sup>)

**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.

**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.

\*\*\*Hepatitis C treatment should not cause pain that requires narcotic pain medication.

**BENEFITS OF TREATMENT**

In most cases, hepatitis C will respond to treatment as determined by a blood test that measures the presence and amount of hepatitis C in the blood. If you have no hepatitis C in your blood 12 weeks **after** the end of treatment, this is called a “sustained virologic response” and means you no longer have hepatitis C. Your chance of achieving a sustained virologic response depends on the hepatitis C genotype, how much hepatitis C virus you have in your blood at the beginning of treatment, any past treatment response, and how much liver damage you have prior to treatment.

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. You may choose to stop treatment at any time.

**In Studies:**

Persons with genotype 1 without cirrhosis who previously failed treatment with a sofosbuvir plus ribavirin containing regimen with or without peginterferon alfa were treated with Harvoni® & ribavirin for 12 weeks and had a 100% response (cure) rate.

Persons with genotype 1 who had cirrhosis and previously failed treatment were treated with Harvoni® and ribavirin for 12 weeks and had a 96% response (cure) rate.

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

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 (Childs-Pugh B) had an 87% response rate. Those with genotype 1 who had advanced cirrhosis (severe/Childs-Pugh C) had an 88% response rate after a 12-week treatment course of Harvoni® and ribavirin.

### **WHOM TO CALL**

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

