Epclusa® (Sofosbuvir/Velpatasvir) & 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.

On June 28, 2016 the FDA approved sofosbuvir combined with velpatasvir in one tablet (Epclusa®) for the treatment of hepatitis C genotypes 1-6. In some circumstances, it has been found that the treatment works better when given with ribavirin.

Treatment with Epclusa® 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 10 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:

____ Epclusa® & weight-based ribavirin will be given for 12 weeks if:

□ You have genotype 1, 2, 3, 4, 5, or 6 with decompensated cirrhosis (Child-Pugh Class B or C).

□ You have genotype 3 with pre-treatment NS5A resistance associated polymorphisms.

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

Epclusa® is a fixed-dose combination tablet containing sofosbuvir 400mg and velpatasvir 100mg. You will take Epclusa® 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 Epclusa® in a day. Take your next dose at your regular time the next day.

- The most common side effects in clinical trials were headache (22%), feeling tired/fatigue (15%), and nausea (9%).

Tell your healthcare provider if you are taking any of the following medicines, as they are not recommended to be used with Epclusa® (this list is not all inclusive, medicines that are P-gp inducers and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4 are not recommended):

- Co-administration of proton-pump inhibitors (once daily medications for indigestion, heartburn, or stomach ulcers) is not recommended. If medically necessary omeprazole (Prilosec®) no more than 20 mg daily is okay taken 4 hours after Epclusa®. In this case, Epclusa® should be taken with food. Esomeprazole (Nexium®), lansoprazole (Prevacid®), rabeprazole (Aciphex®), and pantoprazole (Protonix®) have not been studied with Epclusa®.
- Amiodarone (Cordarone®, Nexterone®, Pacerone®)
- Carbamazepine (Carbatrol®, Epitol®, Equetro®, Tegretol®)
- Efavirenz (ATRIPLA®)
- Oxycarbazepine (Trileptal®, Oxtellar XR®); Phenytoin (Dilantin®, Phenytek®); Phenobarbital (Luminal®); Primidone (Mysoline®)
- Rifabutin (Mycobutin®); Rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®); Rifapentine (Priftin®)
- St. John's wort (Hypericum perforatum) or a product that contains St. John's wort
- Tipranavir (Aptivus®) used in combination with ritonavir (Norvir®)
- Topotecan (Hycamtin®)

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 Rolaids®, Maalox® and Mylanta®) must be taken 4 hours before or 4 hours after you take Epclusa®.
- Twice daily medicine for indigestion, heartburn, or stomach ulcers must be taken at the same time or 12 hours apart from Epclusa®. Famotidine (Pepcid AC®) no more than 40 mg twice daily is okay. Nizatidine (Axid®), cimetidine (Tagamet®), and ranitidine (Zantac®) have not been studied with Epclusa®.
- Digoxin (Lanoxin®)
- Regimens containing tenofovir disproxil fumarate (DF) (ATRIPLA®, COMPLERA®, STRIBILD®, TRUVADA®, VIREAD®)
- Rosuvastatin (Crestor®) Do not exceed 10mg. Monitor for myopathy and rhabdomyolysis.
- Atorvastatin (Lipitor®) Monitor for myopathy and rhabdomyolysis.

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 Epclusa® & 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 does 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 Clinical Trials:

The overall treatment response (cure) rate for Epclusa® and ribavirin given for 12 weeks was 94% for persons with hepatitis C genotypes 1, 2, 3, and 4 with decompensated cirrhosis (Child-Pugh B or C) who were never treated before or were treated in the past with peginterferon and ribavirin with or without a protease inhibitor (ASTRAL-4).

Persons with genotype 1a had a 94% (51/54) response rate.

Those with genotype 1b had a 100% (14/14) response rate.

Persons with genotype 2 had a 100% (4/4) response rate.

Those with genotype 3 had an 85% (11/13) response rate.

Persons with genotype 4 had a 100% (2/2) response rate.

Genotype 3 subjects with pretreatment Y93H resistance associated polymorphisms (RAPs) treated for 12 weeks with Epclusa® had an 80% response rate. Those with compensated cirrhosis and pretreatment RAPs had a 67% response rate. It is expected that the sustained virologic response rate will improve with the addition of 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.

TREATMENT AGREEMENT

To receive treatment, please review the following statements and initial beside the responses:

_____ I agree not to drink alcohol or use recreational drugs during the treatment.

_____ I will tell my provider if I have any serious medical conditions (such as heart disease, high blood pressure, diabetes, high cholesterol, rheumatoid arthritis, or drug addiction), or psychiatric conditions (depression, history of suicide attempts, bipolar disorder, or psychosis).

_____ I am willing to visit the clinic and see a provider on a regular schedule for the entire length of the treatment. If I am unable to attend an appointment, I will let my provider know this ahead of time and I will reschedule my appointment.

_____ I understand that my treatment will be stopped if I cannot attend appointments as required for evaluation of my health and well-being during treatment and the effectiveness of treatment.

_____ I will use 2 acceptable methods of birth control during treatment and for 6 months after I stop treatment (see lists, page 1).

_____ As a female, I understand that I cannot be pregnant or breastfeeding during the treatment and for 6 months after treatment. I understand that my treatment will be stopped if I become pregnant. ____ Not applicable, I am surgically sterile or post-menopausal.

_____ As a male taking ribavirin I understand that I should not father a child during treatment and for 6 months after treatment.

_____If I have any problems with the medications or side effects that bother me, I will let my provider or nurse know right away.

_____ I understand that my hepatitis C may not respond to treatment.

_____ I understand that my provider can stop my treatment if the provider feels that stopping it is in the best interest of my health and welfare.

_____ I will do my best to take my medications as prescribed by my provider. If I am unable to do so, I will contact my provider.

_____ I will protect myself and others from hepatitis C by not sharing needles, toothbrushes, razors or nail clippers and covering cuts to prevent blood exposure.

My signature below means that I have read this treatment agreement and/or the meaning of the information has been explained to me. I agree to treatment.

_____

Patient's Name (PLEASE PRINT) **Patient's Signature** **Date**

_____

Provider's Name (PLEASE PRINT) **Provider's Signature** **Date**