HEPATITIS C 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.

In December 2013, the FDA approved sofosbuvir in combination with ribavirin (genotypes 2 & 3) and sofosbuvir in combination with peginterferon and ribavirin (genotypes 1 & 4) for the treatment of hepatitis C. The American Association for the Study of Liver Diseases (AASLD) and Infectious Disease Society of America (IDSA) developed hepatitis C guidelines post-FDA approval of sofosbuvir for all genotypes (including genotypes 5 & 6) and encompassing re-treatment.
The entire treatment requires 7 scheduled visits over a 6-month period if you undergo a 12-week treatment course. If you undergo a 24-week treatment course, there are approximately 10 scheduled visits over 9 months.

PREGNANCY WARNING
This treatment can harm an unborn child or breastfeeding infant. A woman must not get pregnant and a man should not father a child during treatment or for 6 months after treatment.

Acceptable Birth Control Methods During Treatment
Use 2 of the following methods:

- Male condom
- Female condom
- Diaphragm
- Cervical cap
- Spermicidal jelly
- A non-hormonal intrauterine device (IUD)
- Today® vaginal sponge

Unacceptable Birth Control During Treatment
There are no data on the effectiveness of any hormone-containing birth control including birth control pills, patches, Depo shots or implants, or the vaginal ring in women taking sofosbuvir. Therefore 2 non-hormonal methods of birth control (listed above) should be used during treatment with sofosbuvir.

Acceptable Birth Control Methods After Treatment
Use 2 of the following methods:

- Any of the above listed non-hormonal methods
- Birth control pills
- Other hormone-containing birth control

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HOW THE TREATMENT PROCESS WORKS

You will be asked to give a medical history and have a complete medical examination. You may need to have an eye examination, an ECG (a tracing by machine that shows how well your heart is working), and/or a cardiac stress test, if your provider thinks these tests are needed.

You will have blood and urine tests.

- These tests will include a pregnancy test for female patients - a urine pregnancy test will be done monthly during a clinic visit. It is recommended that females who undergo hepatitis C treatment or female partners of males who undergo hepatitis C treatment continue monthly home pregnancy testing for 6 months after treatment and notify their healthcare provider if they become pregnant.

- For those who will be given peginterferon, a genetic blood test, called IL-28b genotype, will be drawn prior to treatment. This test predicts how well someone responds to interferon-based treatment. CC genotype responds better than CT or TT.

- Random drug and alcohol tests may be requested.

You will be given information about the role of liver biopsy in hepatitis C. A liver biopsy may be recommended prior to treatment.

If you have a history of depression or other psychiatric conditions, you may be asked to see a mental health provider before hepatitis C treatment consideration.

Liver Clinic Provider, check one of the following:

_____ You will take sofosbuvir plus peginterferon and ribavirin for 12 weeks if you have genotype 1, 4, 5 or 6 hepatitis C and are able to take interferon. Peginterferon will be given once a week by injection (a shot). You or a family member will be taught how to give the shots.

_____ For persons with genotype 1 who cannot take peginterferon, 24 weeks of sofosbuvir plus ribavirin can be given instead of above treatment.

_____ You will take sofosbuvir plus ribavirin for 12 weeks if you have genotype 2.

_____ You will take sofosbuvir plus ribavirin for 24 weeks if you have genotype 3 hepatitis C.

_____ For persons with genotype 3 who can take peginterferon, 12 weeks of sofosbuvir plus ribavirin and peginterferon can be given instead of above treatment.

_____ You will take sofosbuvir daily for 12 weeks and peginterferon and ribavirin for 24 weeks (recommended for some patients who previously failed treatment).

The first four visits will be at the start of treatment (week 0), and at weeks 1, 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.**

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.

You will have follow-up 3 months and up to 5 years after treatment completion.

TREATMENT MEDICATIONS AND SIDE EFFECTS

Sofosbuvir is a 400mg tablet. You will take sofosbuvir 1 time each day with or without food. Store sofosbuvir at room temperature. If you miss a dose of sofosbuvir, take the missed dose as soon as you remember the same day. Do not take more than 1 tablet of sofosbuvir in a day. Take your next dose of sofosbuvir at your regular time the next day.

- Most common side effects are feeling tired, headache, nausea, trouble sleeping, and itching.

Tell your healthcare provider if you are taking any of the following medications as these may interact with sofosbuvir and affect treatment response or alter your response to one of these medications:

- Carbamazepine (Carbatrol®, Epitol®, Equetro®, Tegretol®)
- Oxycarbazepine (Trileptal, Oxtellar XR™)
- Phenytoin (Dilantin®, Phenytek®)
- Phenobarbitol (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®)/Ritonavir

Ribavirin – This medication comes in a 200mg capsule or tablet. You must take 5 or 6 ribavirin pills daily (based on your weight) divided between two doses (morning and night) with food. 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. The 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), this anemia may make the problem worse, leading to chest pain or heart attack. If your doctor 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, 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.

Peginterferon is given with a short needle just under the skin of the abdomen. You may have pain and redness where the needle goes into the skin.

- Most common side effects are flu-like symptoms - fever, chills, body aches, feeling tired, nausea, headache, and poor appetite. These happen in almost all persons with the first 1 to 3 doses of peginterferon. After that they may go away or lessen, but sometimes these symptoms continue throughout the treatment course. Your white blood count and/or blood platelet count may decrease (go down) while you are taking peginterferon. White blood cells help protect the body from infections and platelets help your blood clot. You may also get a skin rash.

- Less common side effects are diarrhea, vomiting, temporary hair loss, nervousness, dizziness, confusion, and depression. Severe depression and, more rarely, suicide have been reported in persons treated with peginterferon. Some people taking peginterferon have had lung problems, pneumonia, stroke, heart attack, and liver problems; some people have died from these illnesses. Other side effects that can occur include bleeding in parts of your eye. A rarely reported side effect from peginterferon is visual loss.

- **If at any time during treatment you have a change/loss of vision, stop treatment immediately, notify the Liver Clinic, and go to the emergency room.**

- A small percentage of patients treated with peginterferon have developed thyroid problems (either an overactive or underactive thyroid) which have required treatment. These types of thyroid problems can be controlled with medications but treatment may have to be lifelong.

- It is not known whether peginterferon can cause harm to a pregnant woman and/or the unborn child, or whether it can affect the ability of a woman to become pregnant or a man to father a child.

PLEASE NOTE:

You must let your medical, mental health and dental providers, and pharmacist(s) know that you are on treatment medications 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. If you have pain and feel that you need narcotic pain medications, you will need to see your primary care provider. Prescribing of narcotic pain medications will be left up to your primary care provider's discretion.

BENEFITS OF TREATMENT

Your hepatitis C may respond well to treatment, as determined by a blood test which 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 considered a "sustained virologic response" and, in 99% of persons is a cure. Your chance of achieving a sustained virologic response depends on hepatitis C genotype, how much hepatitis C virus you have in your blood at the beginning of treatment, past treatment response, IL-28b genotype, and how much liver damage you have had 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:

Persons with genotype 1 who were treatment-naïve (never treated before) and did not have cirrhosis and were treated with sofosbuvir in combination with peginterferon and ribavirin for 12 weeks had a 90% response (cure) rate. Persons who were treatment-naïve genotype 1 with cirrhosis, had an 80% response rate. Those with multiple factors that affect treatment (advanced fibrosis, IL-28b CT or TT genotype (see explanation of test page 2), virus > 800,000 IU/ml) had a 71% response rate. Those who failed previous peginterferon/ribavirin therapy are expected to have approximately this same rate of cure (71%) based on computer modeling.

Persons with genotype 1 who were treatment-naïve and were given sofosbuvir plus ribavirin (no peginterferon) for up to 24 weeks had response rates from 50-84% in clinical trials with an overall response rate of 72%.

Persons with genotype 2 who were treatment naïve had a ≥ 95% chance of achieving a sustained virologic response from sofosbuvir and ribavirin for 12 weeks. Those with cirrhosis had a response rate of 83% in clinical trials.

Persons with genotype 3 who were treatment-naïve, regardless of cirrhosis status had a ≥ 92% response rate to sofosbuvir in combination with ribavirin for 24 weeks. For those who were treatment-experienced, the response rate was 77% and treatment-experienced with cirrhosis, the response rate was 60%. Persons with genotype 3 who were treatment-naïve and were given sofosbuvir in combination with peginterferon and ribavirin (4 to 12 weeks) had a 97% response rate (39 patients studied).

Persons with genotype 4 who were treatment-naïve had a 96% response rate to sofosbuvir in combination with peginterferon and ribavirin for 12 weeks. Note, the number of genotype 4 patients in clinical trials was small (28 patients studied).

Few data from clinical trials are available for genotypes 5 and 6. Therefore if patients with genotype 5 or 6 need immediate treatment, daily sofosbuvir in combination with peginterferon and ribavirin therapy for 12 weeks is recommended by the American Association for the Study

of Liver Diseases (AASLD) and Infectious Disease Society of America (IDSA). No data supports use of a peginterferon-free treatment regimen for those with genotype 5 or 6.

WHOM TO CALL

If you have any questions about your 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 have not abused alcohol or other substances (intravenous drugs, cocaine, prescription pain medications) within the last 6 months.

_____ 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). Failure to tell my provider about my medical and psychiatric conditions can have life-threatening consequences during this treatment.

_____ 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 the Liver Clinic 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 to evaluate 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, I understand that I should not father a child during treatment and for 6 months after treatment. I understand that I need to use 2 methods of birth control (see list, page 1) because this treatment can cause harm to a baby I father during treatment and up to 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.

HEPATITIS C TREATMENT AGREEMENT

_____ 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 pursue the treatment.

Patient's Name (PLEASE PRINT)

Patient's Signature **Date**

Provider's Signature/Title **Date**