

Zepatier™ (Elbasvir/Grazoprevir) & Ribavirin Treatment Agreement

Liver Disease & Hepatitis Program Providers: Brian McMahon, MD; Youssef Barbour, MD; Lisa Townshend-Bulson, FNP-C; Annette Hewitt, FNP-C; Prabhu Gounder, MD; Ellen Provost, DO; Timothy Thomas, MD; 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 sign the form.

In January 2016 the FDA approved elbasvir combined with grazoprevir in one tablet (Zepatier™) for the treatment of hepatitis C genotypes 1 and 4. In some circumstances, it has been found that the treatment works better when given with ribavirin.

Treatment with Zepatier™ and ribavirin requires 6 scheduled visits over a 6 month period for a 12-week treatment course. If you undergo a 16-week treatment course, there are 7 scheduled visits over 7 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 (must use 2):

- 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:

_____ Zepatier™ & ribavirin will be given for 12 weeks if you have genotype 1a or 1b and have had previous treatment peginterferon, ribavirin and a protease inhibitor (boceprevir, simeprevir, or telaprevir).

_____ Zepatier™ & ribavirin will be given for 16 weeks if you have genotype 1a with baseline NS5A polymorphisms (mutations in the hepatitis C virus that can decrease response to treatment) or genotype 4 and past treatment with peginterferon and ribavirin that failed.

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

Zepatier™ is a fixed-dose combination tablet containing elbasvir 50mg and grazoprevir 100mg. You will take Zepatier™ 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 Zepatier™ in a day. Take your next dose at your regular time the next day.

- The most common side effects are ALT (a liver enzyme) elevation, tiredness, nausea, and headache.

Tell your healthcare provider if you are taking any of the following medicines, as they are contraindicated with Zepatier™ (this list is not all inclusive; medications that are OATP1B1/3 inhibitors or strong CYP3A inducers are contraindicated):

- Phenytoin (Dilantin®, Phenytek®)
- Carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol® XR)
- Rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®)
- St. John's wort (*Hypericum perforatum*) or a product that contains St. John's wort
- Efavirenz (ATRIPLA®, Sustiva®); Tipranavir (Aptivus®); Atazanavir (Reyataz®, Evotaz™); Darunavir (Prezista®, Prezcobix®); Lopinavir/ritonavir (Kaletra®); Saquinavir (Invirase®); Etravirine (Intelence®)
- Cyclosporine (Gengraf®, Neoral®, Sandimmune®)

Tell your healthcare provider if you are taking any of the following medicines, as they are not recommended to be used with Zepatier™ (this list is not all inclusive; medications that are moderate CYP3A inducers are not recommended):

- Nafcillin
- Ketoconazole
- Bosentan (Tracleer®)
- Modafinil (Provigil®)
- Cobicistat containing regimens: elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate or alafenamide (Stribild®, Genvoya®)

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

- Tacrolimus (Astagraf XL®, Envarsus XR™, FK506 (common name), Hecoria™, Prograf®)

- Cholesterol lowering medications: atorvastatin (Lipitor®), rosuvastatin (Crestor®), fluvastatin (Lescol®), lovastatin (Mevacor®, Altoprev®), simvastatin (Zocor®)

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 Zepatier™ & 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 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 Studies:

Six persons with genotype 1a with baseline NS5A polymorphisms (mutations in the hepatitis C virus that can decrease response to treatment) treated with Zepatier™ and ribavirin for 16 weeks had a 100% response (cure) rate.

Persons who had genotype 1a or 1b previously treated with Peg-interferon, ribavirin and a protease inhibitor (boceprevir, simeprevir, or telaprevir) and took Zepatier™ and ribavirin for 12 weeks had an overall 96% response (cure) rate.

Five persons with genotype 4 whose previous treatment with peginterferon and ribavirin failed, took Zepatier™ and ribavirin for 16 weeks and had a 100% response (cure) rate.

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.

