

Daklinza™ (Daclatasvir), Sovaldi® (Sofosbuvir), & 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 July 2015 the FDA approved daclatasvir (Daklinza™) in combination with sofosbuvir (Sovaldi®) for the treatment of hepatitis C genotypes 1 and 3. In some circumstances, it has been found that the treatment works better when given with ribavirin.

Treatment with daclatasvir, sofosbuvir, and ribavirin requires approximately 6 scheduled visits over 6 months for a 12-week treatment course and 10 scheduled visits over 9 months for the 24-week treatment course.

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 length and rationale for treatment course of daclatasvir, sofosbuvir, plus ribavirin

___ will be treated for 12 weeks

- you have genotype 1 or 3 with decompensated (severe) cirrhosis

___ will be treated for 24 weeks

- You have genotype 3 without cirrhosis and previous treatment with sofosbuvir/ribavirin failed
- You have genotype 3 with compensated cirrhosis and previous treatment with sofosbuvir and ribavirin or peginterferon and ribavirin failed.
- You have genotype 3 and compensated cirrhosis

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

Daclatasvir is a 60 mg tablet. You will take daclatasvir once daily by mouth with or without food. Store daclatasvir at room temperature. If you miss a dose of daclatasvir, take the missed dose as soon as you remember the same day. Do not take more than 1 tablet of daclatasvir in a day. Take your next dose of daclatasvir at your regular time the next day.

- The most common side effects are headache and tiredness.

Tell your healthcare provider if you are taking any of the following medicines, as they are contraindicated with daclatasvir:

- Rifampin (Rifadin[®], Rifamate[®], Rifater[®], Rimactane[®])
- St. John's wort (hypericum perforatum)
- Phenytoin (Dilantin[®], Phenytek[®]), carbamazepine (Carbatrol[®], Eptol[®], Equetro[®], Tegretol[®])

Tell your healthcare provider if you are taking any of the following medicines, as they are not recommended to be used with daclatasvir:

- Amiodarone (Cordarone[®], Nexterone[®], Pacerone[®])
- Dabigatran etexilate mesylate (Pradaxa[®]); in renal impairment, refer to prescribing information.

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

Drugs that require daclatasvir dose reduction to 30mg:

- Atazanavir/ritonavir (Reyataz[®])

- Indinavir (Crixivan®)
- Nelfinavir mesylate (Viracept®)
- Saquinavir mesylate (Invirase®)
- Cobicistat-containing antiretroviral regimens (except darunavir/cobicistat)
- Clarithromycin (Biaxin®)
- Telithromycin (Ketek®)
- Itraconazole (Onmel®, Sporanox®)
- Ketoconazole
- Posaconazole (Noxafil®)
- Voriconazole (Vfend®)
- Nefazodone (Serzone®)

Drugs that require daclatasvir dose increase to 90mg:

- Efavirenz (Sustiva®); Etravirine (Intelence®)
- Nevirapine (Viramune®)
- Nafcillin
- Bosentan (Tracleer®)
- Dexamethasone (Decadron®)
- Modafinil (Provigil®)
- Rifapentine (Priftin®)

Drugs that are moderate CYP3A inhibitors and require monitoring for side effects or drug level*:

- Digoxin (Lanoxicaps®, Lanoxin®) – *Dose reduction recommended and monitor digoxin level while on treatment
- Buprenorphine (Buprenex®, Butrans®, Belbuca™, Subutex®)
- Buprenorphine/Naloxone (Zubsolv®, Bunavail®, Suboxone®)

HMG-CoA Reductase Inhibitors require monitoring for side effects such as myopathy:

- Atorvastatin (Lipitor®); Fluvastatin (Lescol®); Pitavastatin (Livalo®)
- Pravastatin (Pravachol®); Rosuvastatin (Crestor®); Simvastatin (Zocor®)

Sofosbuvir is a 400mg tablet. You will take sofosbuvir once daily by mouth with or without food. Store sofosbuvir 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 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.

Tell your healthcare provider if you are taking any of the following medicines:

- Amiodarone (Cordarone[®], Nexterone[®], Pacerone[®])
- Carbamazepine (Carbatrol[®], Epitol[®], Equetro[®], Tegretol[®])
- 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[®])

Ribavirin is a 200mg capsule or tablet. You will take ribavirin pills twice daily by mouth with food (dose is based on your weight). 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 daclatasvir and sofosbuvir 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:

Persons who were genotype 1 with decompensated (severe) cirrhosis who were treated with daclatasvir and sofosbuvir with ribavirin for 12 weeks had a response rate of 83%. The response rate in those who were Child-Pugh B was 94% and in those whose cirrhosis was Child-Pugh C the response was 56%. Those who had Genotype 3 with decompensated cirrhosis had an 83% response.

Persons with genotype 3 who had compensated (mild) cirrhosis were treated with daclatasvir and sofosbuvir for 12 weeks and had a 58% response. The European compassionate-use

program treated persons with genotype 3 and cirrhosis for 24 weeks with daclatasvir and sofosbuvir and had an 86% response. Pending further data treatment extension and the addition of ribavirin is recommended.

Persons with genotype 3 without cirrhosis who had previous treatment with sofosbuvir plus ribavirin that failed were treated with daclatasvir and sofosbuvir for 12 weeks and had a 71% response. Based on this limited data it is recommended to extend treatment duration to 24 weeks and add ribavirin.

There is limited data for retreating persons with genotype 3 and cirrhosis whose previous treatment has failed. Genotype 3 cirrhotic patients given daclatasvir and sofosbuvir with ribavirin for 12 or 16 weeks had an 88% and 89% response rate. Therefore, it is recommended that persons with genotype 3 and compensated (mild) cirrhosis whose previous treatment with sofosbuvir plus ribavirin or peginterferon and ribavirin failed receive daclatasvir plus sofosbuvir and ribavirin for 24 weeks pending additional data.

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.

