



ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

Liver Disease & Hepatitis Program
4315 Diplomacy Drive, Anchorage, AK 99508
Phone: 907-729-1560 Fax: 907-729-1570
Website: <http://www.anthc.org/hep>

We are glad to hear you are interested in treatment for hepatitis C!

Here are some things to think about (and do) before you make your final decision about treatment:

Why do treatment now? New medicines have increased the chance of cure and have fewer side effects.

Some people have worse liver disease than others. If you have more severe liver disease (a lot of scarring in the liver or cirrhosis) you should consider getting treatment sooner.

What will happen during treatment?

There are 2 medication options for **genotype 1**:

- Option 1 is Harvoni® (ledipasvir/sofosbuvir), 1 tablet taken once a day for 8- 12 weeks. 24 weeks of treatment is required for some persons with significant cirrhosis AND persons with cirrhosis who had previous treatment that failed. The most common side effects include feeling tired and headache. In clinical studies, treatment response rates for Harvoni® were 94-100%.
- Option 2 is Viekira Pak® (ombitasvir, paritaprevir, and ritonavir tablets; dasabuvir tablets) co-packaged as 3 tablets in the morning and 1 tablet in the evening with food. Most treatments with Viekira Pak® also require ribavirin, which is 5-6 additional tablets divided between morning and evening with food. Treatment length is 12 to 24 weeks. The major side effects include feeling tired, nausea, itching and skin rash, trouble sleeping and weakness. A common side effect of ribavirin is anemia. In clinical studies, treatment response rates for Viekira Pak® and Viekira Pak®/ribavirin were 86-100%.

Genotype 2 treatment is Sovaldi® (sofosbuvir), 1 tablet taken once a day and 5-6 ribavirin capsules divided between morning and evening with food for 12 weeks. The major side effects include feeling tired, headache, nausea, insomnia, weakness, itching, diarrhea, and irritability. A common side effect of ribavirin is anemia. In clinical studies, treatment response rates for Sovaldi®/ribavirin were 82-100%.

There are 3 medication options for **genotype 3**:

- Option 1 is Sovaldi® (sofosbuvir), 1 tablet once a day and 5-6 ribavirin capsules divided between morning and evening with food for 24 weeks. The major side effects are listed above under genotype 2 treatment. In clinical studies, treatment response rates for Sovaldi®/ribavirin were 60% -93%.
- Option 2 is Daklinza® (daclatasvir) and Sovaldi® (sofosbuvir) 1 tablet of each taken once daily for 12 weeks. 24 weeks of treatment is required for persons with cirrhosis AND

persons with cirrhosis who had previous treatment that failed. The most common side effects are headache and fatigue. In clinical studies, treatment response rates for Daklinza® and Sovaldi® were 58-98%.

- Another Genotype 3 treatment option for those who can take peginterferon, is 12 weeks of Sovaldi® (sofosbuvir) plus ribavirin (6-7 pills/day), and a weekly peginterferon injection. In addition to the side effects occurring with Sovaldi®/ribavirin treatment additional side effects include flu-like symptoms, depression and body aches, and side effects that may show up only in blood tests. In a clinical study, this treatment resulted in a treatment response rate of 83%.

PLEASE NOTE: Ribavirin cannot be given to a pregnant or breastfeeding female or to a female who plans to become pregnant or a male who plans to father a child during treatment and for 6 months after treatment because it can cause birth defects. There are no studies on Harvoni®, Sovaldi®, Viekira Pak® or Daklinza® in pregnant women or nursing mothers. Safety/risk during pregnancy or breastfeeding has not been established.

Are you ready for treatment?

To ensure that you will be successful in completing hepatitis C treatment we ask that the following items be done before starting treatment. We will review them together.

- You must be alcohol and drug-free. If you have recent drug/alcohol abuse, you need to be in an approved drug treatment program.
- You need to discuss hepatitis C treatment with your primary care provider and get his or her “OK” to start treatment. Your family medicine provider can help you with non-liver related health problems during and after treatment.
- You should have a relative/close friend who is willing to help support you during treatment. If possible, please bring your support person with you to the treatment start appointment.
- You need to be committed to making every treatment appointment and getting **FREQUENT** blood draws (every 1-4 weeks). We will want to follow you very closely during treatment.

Additional Requirements If Checked:

_____ If you have cirrhosis, you may need an EGD (when a doctor looks into your esophagus and stomach for swollen veins that can bleed).

_____ If you have cirrhosis, you need to have an ultrasound of the liver (done in the past 6 months). This ultrasound checks your liver for cancer.

_____ Other: _____

_____ Other: _____

Once everything you need to do on the list has been done, call your primary care provider to make an appointment to plan for hepatitis C treatment. At this appointment, treatment and side effects will be discussed in detail.

Congratulations on completing all the pre-treatment requirements!

Hepatitis C Pre-Treatment Checklist

Before Treatment Starts:

• Labs:

- Immediately prior: ☐ Pregnancy test
☐ Uric Acid (with ribavirin)
- Within 1 month: ☐ Complete Blood Count with differential
☐ Comprehensive Metabolic Panel
(If GFR <30, do not start treatment; consult Liver Disease Specialist)
☐ PT/INR
- Within 3 months: ☐ HCV RNA
☐ Genotype confirmation
- Within 6 months: ☐ AFP
☐ TSH
☐ A1C or Fasting Glucose
☐ Vitamin D 25OH
- Within 1 year: ☐ HIV screening

- **Screen & Review:** AUDIT-C ____ PHQ-9 ____
Drug & Alcohol Screen (at discretion of provider) ____

• Vaccine Status/Screening:

- Hepatitis A & B vaccinations are recommended for all persons with HCV
 - ☐ Hepatitis A (If vaccine status is unknown, check hep A total IgG)
 - ☐ Hepatitis B (If vaccine status is unknown, check HBsAg & HBsAb)
- Other vaccines as appropriate:
 - ☐ Flu (annually)
 - ☐ Pneumococcal-13 (≥ age 65 or high risk/immunosuppressed)
 - ☐ Pneumococcal-23 (≥ age 50 AN/AI living in Alaska or high risk)
 - ☐ Td (once every 10 years) **OR** Tdap (once)
 - ☐ Zoster (≥ age 60)

Pre-Treatment Clinical Evaluation:

- ☐ Medical history including liver disease history and past hepatitis C treatment
 - ☐ Hypertension/Diabetes controlled
 - ☐ Counsel about smoking cessation
 - ☐ Counsel about pregnancy prevention (see Treatment Agreement)
- ☐ Review all medications; check for drug interactions with treatment meds
- ☐ Physical Exam
- ☐ Hepatitis C Treatment Agreement reviewed and signed
- ☐ ECG (If treatment includes ribavirin or peginterferon, over age 65 or h/o cardiac disease)

If treatment includes peginterferon complete the following:

- ☐ Mental Health Evaluation if h/o depression or other psychiatric condition
- ☐ Stress Test (h/o cardiac disease, prior to peginterferon or ribavirin)
- ☐ Dilated retinal/ophthalmology exam (peginterferon candidates only who have HTN, HLD, DM, or h/o retinal disease or blindness)

Sofosbuvir-Based Treatment Symptoms Inventory
(Complete at Weeks 0, 2, 4, and monthly after that)

Are you experiencing any of the following symptoms? Check here if Yes

Feeling excessively tired/fatigued/exhausted	
Trouble Sleeping	
Headache	
Muscle Aches/Pains	
Joint Aches/Pains	
Back pain	
Weakness	
Flu-Like Illness	
Chills	
Fever	
Diarrhea	
Decreased Appetite	
Nausea	
Vomiting	
Weight loss	
Heartburn or upset/sour stomach	
Itching	
Rash Where: _____	
Irritability	
Depression / Anxiety	
Changes in mood/Mood swings	
Feeling forgetful, problems concentrating	
Decreased or blurred vision	
Shortness of breath	
Cough	
Dizziness	
Dry Mouth	
Hair Loss	
Other, specify: _____	
Nurse or Provider to check if yes this week:	
Anemia (Hgb below 10 g/dL)	
Neutropenia (ANC $\leq 0.5 \times 10^9/L$)	
Thrombocytopenia (Plt $< 50 \times 10^9/L$)	
Hypothyroidism/Hyperthyroidism (Specify which)	

Name: _____

Chart #: _____

Weeks of Treatment Completed: _____

Date: _____

Sovaldi® (Sofosbuvir), Ribavirin, & Peginterferon Treatment Agreement

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 American Association for the Study of Liver Diseases (AASLD) and Infectious Disease Society of America (IDSA) developed hepatitis C guidelines for all genotypes (1 through 6) and encompassing re-treatment. The current FDA approved treatment for genotype 4 and some persons with genotype 3 is sofosbuvir in combination with peginterferon and ribavirin.

Treatment with sofosbuvir, ribavirin, and peginterferon requires 6 scheduled visits over a 6 month period if you undergo a 12-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:

- 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.

Treatment Regimen:

_____ Sofosbuvir plus peginterferon and ribavirin will be given for 12 weeks if you have hepatitis C genotype 3, 4, 5, or 6 and are able to take peginterferon.

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 see your primary care provider more frequently if you are having side effects or problems related to the treatment.

You will have follow-up 3 months and annually for 5 years after treatment completion. If you have cirrhosis you should continue to have a liver ultrasound every six months and regular clinic visits.

TREATMENT MEDICATIONS AND SIDE EFFECTS

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 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 medicines:

- Amiodarone (Cordarone®, Nexterone®, Pacerone®)
- Carbamazepine (Carbatrol®, Epitol®, Equetro®, Tegretol®)
- Oxycarbazepine (Trileptal®, Oxtellar XR™)
- Phenytoin (Dilantin®, Phenytek®)
- Phenobarbital (Luminal®)
- 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 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.

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. You or a family member will be taught how to give the injection.

- 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 your provider, 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, dental providers, and pharmacist(s) know that you are taking sofosbuvir, ribavirin, & peginterferon prior to starting any new medications. You must let your healthcare 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

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 Clinical Trials:

Persons with genotype 3 who were treatment-naïve and were given sofosbuvir in combination with peginterferon and ribavirin 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 persons with genotype 5 or 6 need immediate treatment, daily sofosbuvir in combination with peginterferon and ribavirin therapy for 12 weeks is recommended by the AASLD and 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 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 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 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

Sovaldi® (Sofosbuvir), Ribavirin, & Peginterferon 12 week Treatment Checklist

Prior to Treatment

Labs

- Immediately prior: ☐ Uric Acid
☐ Pregnancy test (if applicable)
- Within 1 month: ☐ CBC ^{1, 2}
☐ CMP (If GFR <30, do not start treatment; consult Liver Disease Specialist)
☐ PT/INR
- Within 3 months: ☐ HCV RNA
☐ Genotype confirmation
- Within 6 months: ☐ AFP
☐ TSH
☐ A1C or Fasting Glucose
☐ Vitamin D 25OH (treat if deficient)
- Within 1 year: ☐ HIV screening

Miscellaneous

- ☐ Hepatitis A status/screening if not done
☐ Hepatitis B status/screening if not done
☐ PHQ-9 baseline
☐ AUDIT-C
☐ Symptoms Inventory baseline

Week 2

- ☐ CBC ^{1, 2}
☐ CMP³
☐ Symptoms Inventory

Week 4¹

- ☐ HCV RNA
☐ CBC ^{1, 2}
☐ CMP³
☐ Symptoms Inventory
☐ PHQ-9 ¹
☐ Pregnancy test (if applicable)

Week 8

- ☐ CBC ^{1, 2}
☐ CMP³
☐ Symptoms Inventory
☐ PHQ-9 ¹
☐ Pregnancy test (if applicable)

Week 12

- ☐ HCV RNA
☐ CBC ^{1, 2}
☐ CMP³
☐ TSH ¹
☐ Symptoms Inventory
☐ PHQ-9 ¹
☐ Pregnancy test (if applicable)

3 months post treatment

- ☐ CBC
☐ Liver Function Tests
☐ HCV RNA
☐ PHQ-9

Nurse follow-up in clinic or by phone:

- ☐ Symptoms Inventory
☐ Managing side effects
☐ Medication adherence discussion
☐ Alcohol intake
☐ Birth control reminder
☐ Refill reminder

1- **On** interferon: CBC with auto diff; baseline & monthly PHQ-9; Ophthalmology exam at baseline & 4-6 weeks later.

2- **Not on** interferon: CBC without differential.

3- If GFR <30, consult Liver Disease Specialist.

Sovaldi® (Sofosbuvir), Ribavirin, & Peginterferon 12 week Lab Tracking Form

General Patient Information

Name: _____

DOB: ____/____/____

MRN: _____

Phone #: _____

Treatment Start Date: _____

Lab Results

HCV RNA: _____

Genotype: _____ HIV: ____ TSH: _____

Vit D 25OH: _____ AFP: _____ GFR*: _____

PT/INR: _____ A1C/Glucose: _____

Medication Regimen

1- Sofosbuvir 400mg 1 tablet PO daily. Do not change dose.

2- Ribavirin: _____ mg/day PO divided into 2 doses. Take with breakfast & dinner.
 ≥75kg = 1200mg/day <75kg = 1000mg/day

**Dose Reduction/Date: ____/____ **Additional Dose Change/Date: ____/____

3- PegInterferon (PEG) subcutaneous injection every 7 days.
 Circle which is used: alfa 2a 180mcg (Pegasys/Roche) **or**
 *alfa 2b (PegIntron/Schering) Weight-based dose: _____

**Dose Change/Date: ____/____ **Additional Dose Change/Date: ____/____

*Refer to Hepatitis C Treatment Medications & Dosing form.
 **Consult ANTHC Liver Disease & Hepatitis Specialists for further guidance about dose changes.

Completed Treatment Week	Lab Date	Hgb	Hct	WBC	ANC	PLT	ALT	AST	Alk Phos	Total Bili	Creat/ GFR	PHQ-9 (Baseline & 1 yr post tx; specified weeks if on PEG)	HCV RNA (Specified weeks)	Weight (kg)	Pregnancy Test & TSH (Specified weeks)
Pre-Treatment															
Treatment Start Week 0												PHQ-9	HCV RNA		TSH
<i>optional</i>															
Week 2															
<i>optional</i>															
Week 4												PHQ-9	HCV RNA		
<i>optional</i>															
<i>optional</i>															
Week 8												PHQ-9			
<i>optional</i>															
<i>optional</i>															
Week 12												PHQ-9	HCV RNA		TSH
<i>optional</i>															
3 months post treatment												PHQ-9	HCV RNA		TSH

Labs recommended for each follow up visit: CBC w/diff, CMP, pregnancy test (females of childbearing age), and HCV RNA as specified.

Please note the following critical values. These may require modification of dosage or discontinuation of causative med. Contact ANTHC Liver Disease Specialists with any questions.

***GFR <30** If GFR is <30, do not start treatment; consult with Liver Disease Specialists.

Hgb <10.0 gm/dL If hemoglobin drops below 10, reduce ribavirin dose to 600mg (refer to Sofosbuvir package insert). **If hemoglobin <8.5, hold ribavirin & consult ANTHC Liver Disease Specialists.**

ANC <0.5 K/uL If absolute neutrophil count drops below 0.5, reduce PEG dose (refer to PEG package insert) and consult ANTHC Liver Disease Specialists.

PLTs <50 K/uL If platelet count drops below 50, reduce PEG dose (refer to PEG package insert) and consult ANTHC Liver Disease Specialists. If platelet count <25, permanently discontinue PEG.

GFR <50 If GFR is <50, decrease ribavirin dose (refer to ribavirin package insert) and consult ANTHC Liver Disease Specialists.