



Liver Disease & Hepatitis Program
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Website: <http://www.anthctoday.org/community/hep/index.html>

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.

Why would I wait? Within 1-2 years additional new medicines will be available. They may work even better, shorten treatment time, cost less, 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 by mouth. Treatment length is 12 weeks for most patients. 24 weeks of treatment is required for some persons with decompensated (significant) cirrhosis AND persons with cirrhosis who had previous treatment that failed. The major side effects (experienced in $\geq 10\%$ of clinical trial subjects) 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 depending on genotype subtype and cirrhosis status. 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 and 3 treatment is Sovaldi[®] (sofosbuvir), which is 1 tablet once a day and 5-6 ribavirin capsules divided between morning and evening with food. Treatment length is 12 weeks for genotype 2 and 24 weeks for genotype 3. 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% in genotype 2 and 60% -93% in genotype 3.

- 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 can be given. 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: No treatments containing ribavirin can 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 this treatment can cause birth defects. There are no studies on ledipasvir or sofosbuvir (Harvoni® or Sovaldi®) in pregnant women or nursing mothers. Safety/risk during pregnancy or breastfeeding has not been established.

Are you ready for treatment?

There are several requirements for hepatitis C treatment. These requirements are to ensure that you are going to be successful in completing treatment, and to protect your physical and mental health. The following items must be done before you can start treatment. We will review them together.

- You must be alcohol and drug-free for at least 6 months before you can start treatment.
- 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 or close friend who is willing to help support you during treatment. The person you choose should come with you to the pre-treatment 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). This requires sedation and is done as a Day Surgery procedure. Your primary care provider will make this referral if needed.

_____ 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.

Please bring your support person with you to this appointment.

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 (\geq age 65 or high risk/immunosuppressed)
 - Pneumococcal-23 (\geq age 50 AN/AI living in Alaska or high risk)
 - Td (once every 10 years) **OR** Tdap (once)
 - Zoster (\geq 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)

Viekira Pak® (ombitasvir, paritaprevir, ritonavir; dasabuvir) and ribavirin 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.

In December 2014, the FDA approved ombitasvir, paritaprevir, and ritonavir tablets; dasabuvir tablets co-packaged (Viekira Pak®) to be given with ribavirin for the treatment of hepatitis C genotype 1a with or without cirrhosis and genotype 1b with cirrhosis, including those with HCV/HIV co-infection.

Treatment with Viekira Pak® requires 6 scheduled visits over 6 months if your treatment course is 12 weeks, and 9 scheduled visits over 9 months if your treatment course is 24 weeks.

PREGNANCY & BREASTFEEDING WARNING

It is not known if Viekira Pak® will harm an unborn or breastfeeding baby. However, 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.

You must stop using ethinyl estradiol-containing medicines before you start treatment with Viekira Pak®. If you use these medicines as a method of birth control you must use another method of birth control during treatment with Viekira Pak®, and for about 2 weeks after finishing treatment with Viekira Pak®.

Acceptable Birth Control Methods (must use 2):

- Progestin only contraceptives (e.g. mini pill, Depo shot, Nexplanon®)
- 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.

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.

Provider, select the appropriate treatment regimen:

___ Viekira Pak® & ribavirin for 12 weeks

- genotype 1a without cirrhosis
- genotype 1b with cirrhosis

___ Viekira Pak® & ribavirin for 24 weeks for genotype 1a with cirrhosis

Ribavirin dose is based on weight (1000 mg for persons less than or equal to 75 kg (165 lb) and 1200 mg/day for those greater than 75 kg, divided and taken twice daily with food) except for those post liver transplant, see below.

___ Viekira Pak® & ribavirin for 24 weeks for genotype 1a or 1b post liver transplant with normal hepatic function without cirrhosis (Metavir fibrosis stage F0-F2). Ribavirin dose will start at 600 to 800 mg divided and taken twice daily with food and may be increased as tolerated.

Note: Viekira Pak® is not recommended for persons with moderate cirrhosis (Child-Pugh Class B) and is contraindicated for those with severe cirrhosis (Child-Pugh Class C).

TREATMENT MEDICATIONS AND SIDE EFFECTS

Viekira Pak® contains ombitasvir, paritaprevir, and ritonavir tablets and dasabuvir tablets co-packaged for oral use. Two pink tablets contain ombitasvir 12.5 mg, paritaprevir 75 mg and ritonavir 50 mg and are taken at the same time daily (in the morning) with a meal. Two beige tablets contain dasabuvir 250 mg and one of them is taken twice daily (in the morning and evening) with a meal. Store the medication at room temperature.

If you miss a dose of the pink tablets, and it is less than 12 hours from the time you usually take your dose, take the missed dose with a meal as soon as possible. Take your next dose at your regular time the next day with a meal. If you miss a dose of the pink tablets more than 12 hours from the time you usually take your dose, do not take the missed dose. Take your next dose at your regular time the next day with a meal.

If you miss a dose of the beige tablet and it is less than 6 hours from the time you usually take your dose, take the dose with a meal as soon as possible. Then take your next dose at your regular time with a meal. If it is more than 6 hours since you missed your dose, do not take the missed dose. Instead, take your next dose at your regular time with a meal.

Do not take more than the prescribed dose of Viekira Pak® (no doubling up).

Tell your healthcare provider if you are taking any of the following medicines; contraindicated with Viekira Pak®:

- Alfuzosin hydrochloride (Uroxatral®)
- Carbamazepine (Carbatrol®, Epitol®, Equetro®, Tegretol®)
- Efavirenz (Atripla®, Sustiva®)
- Ergot containing medicines including: ergotamine tartrate (Cafergot®, Ergomar®, Ergostat®, Medihaler®); dihydroergotamine mesylate (D.H.E. 45®, Migranal®); methylergonovine (Ergotrate®, Methergine®)
- Ethinyl estradiol-containing medications; combination birth control pills or patches, such as Lo Loestrin® FE, Norinyl®, Ortho Tri-Cyclen Lo®, Ortho Evra®; hormonal vaginal rings such as Nuva Ring®, hormonal replacement therapy medicine Fem HRT®.
- Gemfibrozil (Lopid®)
- Lovastatin (Advicor®, Altoprev®, Mevacor®)
- Midazolam, when taken by mouth
- Phenytoin (Dilantin®, Phenytek®)
- Phenobarbital (Luminal®)
- Pimozide (Orap®)
- Rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®)
- Sildenafil citrate (Revatio®) when taken for pulmonary artery hypertension
- Simvastatin (Simcor®, Vytorin®, Zocor®)
- St. John's wort (*Hypericum perforatum*) or a product that contains St. John's wort
- Triazolam (Halcion®)

Please tell your health care provider if you are taking the following medications; dosage adjustments or monitoring may be recommended:

- Amiodarone, bepridil, disopyramide, flecainide, lidocaine(systemic), mexilitine, propafenone, quinidine, digoxin
- Ketoconazole
- Voriconazole
- Amlodipine
- Fluticasone
- Furosemide
- Atazanavir/ritonavir once daily, darunavir/ritonavir, lopinavir/ritonavir, rilpivirine
- Rosuvastatin, pravastatin
- Cyclosporine, tacrolimus
- Salmeterol
- Buprenorphine/naloxone
- Omeprazole
- Alprazolam

Ribavirin is a 200mg capsule or tablet. You will take ribavirin pills twice daily by mouth with food (dose is based on your weight, except for those who have had a liver transplant). 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, 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.

The most common side effects of Viekira Pak® given with ribavirin are tiredness, nausea, itching, skin reactions such as redness or rash, sleep problems, and feeling weak.

PLEASE NOTE:

You must let your medical, mental health, dental providers, and pharmacist(s) know that you are taking Viekira Pak® & ribavirin prior to starting any new medications. You must let your health care 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

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, 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 1a who did not have cirrhosis were treated with Viekira Pak® and ribavirin for 12 weeks and had a 96% response (cure) rate.

Those with genotype 1a with cirrhosis treated with Viekira Pak® and ribavirin for 24 weeks had a 93- 100% response rate.

Those with genotype 1b and cirrhosis treated with Viekira Pak® and ribavirin for 12 weeks had a 100% response rate. Persons with genotype 1b and cirrhosis who had been treated in the past had response rates between 86-100%.

WHOM TO CALL

If you have any questions about treatment, your primary care provider at _____.

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).

___ 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/Title Date

HCV 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/Skin Reactions Describe: _____	
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: _____

Viekira Pak® (ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg; dasabuvir 250 mg) & Ribavirin 24 week Treatment Checklist

Prior to Treatment

Labs

- Immediately prior: ___ Pregnancy test (if applicable)
___ Uric Acid
- Within 1 month: ___ CBC
___ CMP (If GFR <50, 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 (with ribavirin)

- ___ CBC
___ CMP¹
___ Symptoms Inventory

Week 4

- ___ HCV RNA
___ CBC
___ CMP¹
___ Symptoms Inventory
___ Pregnancy test (if applicable)

Weeks 8, 12, 16, & 20

- ___ CBC
___ CMP¹
___ Symptoms Inventory
___ Pregnancy test (if applicable)

Week 24

- ___ HCV RNA
___ CBC
___ CMP¹
___ Symptoms Inventory
___ 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- If GFR <50, consult Liver Disease Specialist.

Viekira Pak® (ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg; dasabuvir 250mg) & Ribavirin 24 week Lab Tracking Form

General Patient Information

Name: _____
 DOB: ____/____/____
 MRN: _____
 Phone #: _____
 Treatment Start Date: _____

Pre-Treatment Lab Results

HCV RNA: _____
 Genotype: _____ HIV: ____ TSH: ____
 Vit D 25OH: _____ AFP: _____ GFR: _____
 PT/INR: _____ A1C/Glucose: _____

Medication Regimen

1- Viekira Pak® Do not change dose.
 2 pink tablets of ombitasvir, paritaprevir, ritonavir with breakfast.
 1 beige tablet of dasabuvir with breakfast and 1 with dinner.
 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: _____/_____
 **Consult ANTHC Liver Disease & Hepatitis Specialists for further guidance about dose changes.

Completed Treatment Week	Lab Date	Hgb	Hct	WBC	PLT	ALT	AST	Alk Phos	Total Bili	Creat/ GFR	PHQ-9 <small>(Specified weeks)</small>	HCV RNA <small>(Specified weeks)</small>	Weight (kg)	Pregnancy Test
Pre-Treatment														
Treatment Start Week 0											PHQ-9	HCV RNA		
<i>optional</i>														
Week 2														
<i>optional</i>														
Week 4												HCV RNA		
<i>optional</i>														
<i>optional</i>														
Week 8														
<i>optional</i>														
<i>optional</i>														
Week 12											PHQ-9	HCV RNA		
<i>optional</i>														
Week 16														
<i>optional</i>														
Week 20														
<i>optional</i>														
Week 24											PHQ-9	HCV RNA		
3 months post treatment											PHQ-9	HCV RNA		

Labs recommended for each follow up visit: CBC, 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.

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

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

PLTs <50 K/uL If platelet count drops below 50, consult ANTHC Liver Disease Specialists.