

Hepatitis C Guidelines

DISCUSSION

Recently, questions have arisen regarding the use of the non-formulary protease inhibitors, telaprevir and boceprevir in the management of offenders with Chronic Hepatitis C. In the October 2011 issue of Hepatology, the American Association for the Study of Liver Disease published updated guidelines for the treatment of Chronic Hepatitis C Genotype 1. The guideline states that currently Peg-Interon and Ribavirin are standards of care.

The Virginia Department of Corrections Office of Health Services Unit recognizes that Hepatitis C virus infection represents a potentially serious problem within the correctional environment. Several clinical studies have revealed that Hepatitis C infections often cause chronic disease. A significant number of individuals infected will develop chronic disease. It is unclear how to predict the clinical outcome of chronic Hepatitis C infection in an individual case. Most studies have shown that approximately 80% of persons with chronic Hepatitis C infection will have a mild course without the development of cirrhosis or death from their infection. Of the remaining 20%, a small percentage will develop severe liver disease. The cohort of patients who develop severe liver disease are most likely to benefit from medical treatment.. Numerous clinical studies have shown that several laboratory tests are helpful in predicting the clinical outcomes of individuals with hepatitis C. The selection of offenders for the treatment of hepatitis C will be based on those laboratory tests and other clinical findings.

These Hepatitis C guidelines address the diagnosis of chronic Hepatitis C, identification of other types of liver disease, the screening process for managing offenders with chronic Hepatitis C, patient education materials, and drug dosing recommendations.

When treatment is approved, it will occur at institutions with 16-24 hours nursing staff. Individuals approved for medical treatment will be transferred to an institution with 16 to 24 hours nursing coverage for the duration of their treatment. During evaluation and treatment, a patient can decline further evaluation or treatment. Offenders who elect to discontinue treatment should be counseled regarding their decision to stop treatment.

Currently, drugs available for the Hepatitis C infection can cause severe and occasionally fatal medical complications. Individuals with some medical and mental health conditions are at high risk of developing severe and fatal medical complications. Consequently, the Virginia Department of Corrections attempts to select those individuals most likely to benefit from treatment and to prevent exposing offenders to very toxic medication who have a low probability of benefitting from treatment.

II. SCREENING

- A. Treatment for inmates with Hepatitis C Virus can be a complicated task. Inmates already on PEG-Intron and Ribavirin treatment at the time of incarceration will be eligible to continue treatment.
- B. During intake all offenders will have a complete metabolic profile. Offenders with elevated liver enzymes will undergo tests to determine if they have hepatitis C. Offenders with alanine aminotransferase enzyme levels two times the normal level will undergo tests to determine if they have hepatitis C and if they should undergo treatment for hepatitis C.
- C. Offenders with elevated liver enzymes should have a quantitative HCV RNA Assay. Offenders with a positive HCV RNA Assay (detectable viral load) should be evaluated for hepatitis C treatment. Offenders with a positive HCV RNA Assay who do not undergo treatment should be evaluated annually.

D. Prior to consideration for Hepatitis C treatment, physicians should review carefully the exclusion and inclusion criteria for treatment.

- Medical Treatment Exclusion Criteria
 1. Normal liver enzymes.
 2. Age greater than 60 and less than 18;
 3. Decompensated cirrhosis:
- Ascites
- Esophageal varices
- Albumin <3.0 g/dl
- INR > 1.5
 4. Hypersensitivity to interferons;
 5. Previous treatment failure or relapse with interferons and/or ribavirin;
 6. Solid organ transplantation;
 7. Pregnancy – due to risk of fetal malformations and fetal death. Pregnancy test required prior to initiating therapy;
 8. Hemoglobinopathies, hemolytic anemias, or other severe anemias;
 9. Ischemic cardiovascular disease or cerebrovascular disease;
 10. Renal insufficiency (Creatinine < 1.5, CrCl <50ml/min);
 11. Poor control of major illness:
 - Diabetes
 - Hypertension
 - Asthma or COPO
 - CHF
 - Coronary artery disease
 - Seizures
 - Thyroid disease
 12. Autoimmune diseases other than HIV;
 13. Chronic systemic steroid use;
 14. Current chemotherapy for malignancy;
 15. Refusal of drug rehabilitation treatment;
 16. Life expectancy of less than 20 years;
 17. Thrombocytopenia (platelets <90,000)
 18. Neutropenia (ANC < 1,500);
 19. Hemoglobin less than or equal to 10;
 20. Refusal to accept Hepatitis A and Hepatitis B Vaccine if not immune;
 21. Evidence of new tattoos or body piercing during evaluation/treatment.
- Mental Health Treatment Exclusion Criteria:
 1. Refusal of a required substance abuse program;
 2. Confirmed drug or alcohol use while incarcerated;
 3. History of psychosis or schizoaffective disorder;
 4. Severe personality disorder (especially borderline or psychopathy);
 5. Extrapyrimal neurologic symptoms;
 6. Poorly controlled major depression;
 7. Current suicidal ideation;
 8. History of multiple suicide attempts;
 9. Severe MR (IQ < 50);
 10. Severe dementia.
- Treatment Inclusion Criteria:

1. Offender is not parole eligible and must have greater than 24 months remaining to serve after liver biopsy prior to earliest release date. If an offender has less than 24 months remaining until earliest his release date, refer to Conservative Treatment (Attachment 1)/
2. Absence of decompensated cirrhosis: no evidence of end stage liver disease, such as ascites, jaundice, esophageal varices or poor liver synthetic function (e.g., albumin, <3.0 g/dl, total bilirubin > 1.5 mg/dl, and prothrombin time international normalized ration (NRR) >1.5).
3. Patient must show good compliance with previously prescribed medical regimens.
4. Medical treatment offenders of Hepatitis C in offenders who are co-infected with Hepatitis C and HIV must be done under the supervision of a Hepatologist or an Infectious Disease Specialist.

III. OFFENDERS EXCLUDED FROM TREATMENT

- A. Enroll in chronic care clinic and perform an evaluation annually. The evaluation should include a targeted physical examination, CBC with platelet count, liver function tests, and other tests if indicated.

IV. BASELINE WORKUP FOR OFFENDERS NOT EXCLUDED FROM TREATMENT

- HIV test
- Bilirubin
- AST
- ALT
- Alk Phosphatase
- Cholesterol
- Creatinine
- Albumin
- INR
- WBC
- ANC
- Hct
- Platelets
- Transferrin
- TIBC (in Caucasians only)

- TSH and T4
- ANA
- PT/PTT
- Hbg A1c
- Pregnancy Test for Females

- C. When workup is complete and offender has no contraindications to treatment based on exclusion criteria and laboratory tests; the form for requesting a Fibrosure test should be completed and faxed to DOC Chief Physician or designee at 804-674-3551.
- D. All off-site consultations for Hepatitis C related treatment and follow-up should be faxed to DOC Chief Physician or designee at Office of Health Services at 804.674.3551.
- E. Complete and place HCV Flow Sheet (Attachment 3) in the offender's medical record.

IV. REPORTING

Complete the Epi-1 Form, send the top two copies to your local health department, and place the third copy (pink) in the medical record after it has been taped or stapled to a full size sheet of paper.

V. CONSENTS AND PATIENT EDUCATION

- A. During the baseline work-up:
 - 1. Review, complete and sign Hepatitis C Frequently Asked Questions (Attachment 4).
 - 2. Review the Hepatitis A Vaccine Information Sheet with the patient (Attachment 5, pages 1 and 2), and have the patient sign the Hepatitis A Vaccine Signature Form (Attachment 6).
 - 3. Review the Hepatitis B Vaccine Information Sheet with the patient (Attachment 7, pages 1 and 2), and have patient sign the Hepatitis B Vaccine Signature Form (Attachment 8).
 - 4. Complete and sign Medical Treatment Exclusion Criteria (Attachment 9).
 - 5. Complete and sign Mental Health Treatment Exclusion Criteria (Attachment 10).
 - 6. Review, complete, and sign Patient Information about PEG-Intron/Ribavirin (Attachment 11).
 - 7. Review, complete, and sign Agreement to Accept Treatment Plan (Attachment 12).
 - 8. Complete and sign, Pre-Consent for Liver Biopsy (Attachment 13).
- B. When all forms are complete, place in the offender's medical record.
- C. Hepatitis C treatment failures and relapses are not eligible for treatment.

VI. Fibrosure Test

- A. Order Fibrosure test. Review Fibrosure test results with offender.
 - 2. Stages 2, 3, and 4 qualify for treatment.
 - 3. Stages 0 and 1 repeat Fibrosure test in 4 years.
- B. If patient qualifies for treatment based on Fibrosure test and inclusion/exclusion criteria, proceed to treatment.
- C. If patient does not qualify for treatment based on Fibrosure test, refer to Conservative Treatment (Attachment 1).

VII. EVALUATION PRIOR TO INITIATING PER-INTRON/RIBAVIRIN THERAPY

- A. Transfer patient to a facility with 16-24 hour nursing staff.
- B. Measure weight and vital signs.
- C. Limited physical exam performed by facility physician to include:
 - 1. Eye exam.
 - 2. Skin exam for jaundice.
 - 3. Abdominal exam for organomegaly, ascites, tenderness.
 - 4. Appropriate exam for co-existing medical conditions.
- D. Hepatitis A and Hepatitis B Vaccine:
 - 1. All Hepatitis C positive offenders should be offered Hepatitis A and Hepatitis B vaccine if not immune.
 - 2. Prior to administration of the vaccine, provide the offender with the Hepatitis A and Hepatitis B Vaccine Information Statements (VIS) (Attachments 5 and 7). Allow time for patient to read the information and ask questions prior to administration of the vaccine.

3. As part of the patient's permanent immunization record, complete the Hepatitis A and Hepatitis B Signature Forms (Attachment 6 and 8). Place the completed forms in the medical record behind the immunization record. Also note the Hepatitis A and Hepatitis B vaccines on the Immunization Record (DOC 724) and HCV Flow Sheet (Attachment 3).

VIII. ADMINISTRATION AND DOSING

A. PEG-Intron/Ribavirin will be administered as follows:

1. PEG-Intron – 1.5 mcg/Kg of body weight once weekly to a maximum dose of 150 mcg according to the following regimen:

Body Weight – kg (lb)	PEG-Intron Vial Strength	Amount of PEG-Intron (mcg) To Administer	Volume (ml) of PEG-Intron to Administer
<40kg (<88)	50mcg/0.5ml	50 mcg	0.5ml
40-50kg (88-110)	80mcg/0.5ml	64mcg	0.4ml
51-60kg (112-110)	80mcg/0.5ml	80mcg	0.5ml
61-75kg (134-165)	120mcg/0.5ml	96mcg	0.4ml
76-85kg (167-187)	120mcg/0.5ml	120mcg	0.5ml
>85kg (>187)	150mcg/0.5ml	150mcg	0.5ml

- Administer as late in the day as possible.
- Give with each dose of PEG-Intron as needed for a maximum of three days:
-Acetaminophen (Tylenol) 325mg-2tablets tid or

-Ibuprofen (Motrin) 200mg – 2 tablets tid.

2. Ribavirin – compounded Ribavirin must be order using Ribavirin Order Form b

(Attachment 14). Ribavirin should not be ordered or administered as monotherapy.

a. Hepatitis C Genotype 1 or 4, 1000 mg to 1200 mg daily in divided doses (maximum 1200 mg daily) based on body weight:

- Less than or equal to (<) 75kg body weight: two 200 mg capsules (400 mg) in the AM and three 200 mg capsules (600 mg) in the PM.
- Greater than (>) 75kg body weight: three 200 mg capsules (600 mg) in the AM and PM.

b. Hepatitis C Genotype 2 or 3, 800 mg daily in divided doses regardless of body weight:

Give two 200 mg capsules (400 mg) in the AM and PM for six months.

B. Required Lab Testing During Treatment and Follow-up:

@	Beginning	of 2 nd Week	CBC, LFT
@	Beginning	of 4 th Week	CBC, LFT, TSH/T4, Doctor Visit after tests back
@	Beginning	of 2 nd Month	CBC, LFT, Doctor Visit
@	Beginning	of 3 rd Month	CBC, LFT, TSH/TA
@	Beginning	of 4 th Month	CBC, LFT, Hep C Quantasure Plus, Doctor Visit
@	Beginning	of 5 th Month	CBC, LFT
@	Beginning	of 6 th Month	CBC, LFT, TSH/T4, Doctor Visit
@	Beginning	of 7 th Month	CBC, LFT, Quantasure Plus for Genotype 1
@	Beginning	of 8 th Month	CBC, LFT
@	Beginning	of 9 th Month	CBC, LFT, TSH/T4, Doctor Visit
@	Beginning	of 10 th Month	CBC, LFT
@	Beginning	of 11 th Month	CBC, LFT
@	Beginning	of 12 th Month	CBC, LFT, TSH/T4, Hep C Quantasure Plus, Doctor Visit
@	End of Treatment		HVC Quantasure Plus, ALT
@	6 month later		HVC Quantasure Plus, ALT

C. Duration of Therapy:

1. Genotype 2 or 3 – 6 months of combination drug therapy.
2. Genotype 1 or 4; begin combination therapy. If HCV RNA is undetectable or shows a minimum of 2-log reduction in viral load from pre-treatment levels at three months, continue therapy for a total of 6 months. If Hep C Quantasure Plus remains positive after 6 months discontinue therapy. If negative, continue therapy for 12 months.

D. Based on routine laboratory testing during treatment, the dose of one or both components of PEG-Intron/Ribavirin therapy may need to be adjusted according to table below:

Guideline for Dose Modification and Discontinuation of PEG-Intron or PEG-Intron/Ribavirin for Hematologic Toxicity

Laboratory	Values	PEG-Intron	Ribavirin
Hemoglobin (HGB)*	<10.0 g/dL <8.5 g/dl	Permanently discontinue	<u>Decrease dose by 200 mg/day</u> Permanently discontinue
WBC	<1.5x10 ⁹ /L <1.0 10 ⁹ /L	<u>Reduce by 50%</u> Permanently discontinue	<u>Decrease dose by 200 mg/day</u> Permanently discontinue
Neutrophils	<0.75x10 ⁹ /L <0.5x10 ⁹ /L	<u>Reduce by 50%</u> Permanently discontinue	Permanently discontinue
Platelets	<80x10 ⁹ /L <50x10 ⁹ /L	<u>Reduce by 50%</u> Permanently discontinue	Permanently discontinue
Bili-direct:	>2.5 x upper limit of normal	Permanently discontinue	Permanently discontinue
Bili-indirect**	>5mg/ml >4 mg/ml	<u>See Below**</u> See Below**	<u>See Below**</u> See Below**
Creatinine	>2.0 mg/dL	Permanently discontinue	Permanently discontinue
ALT and AST	>2 x baseline and/or 10 x upper limit of normal	Permanently discontinue	Permanently discontinue

*For patients with a history of stable cardiac disease receiving PEG-Intron in combination with Ribavirin, the PEG-Intron dose should be reduced to half and the Ribavirin dose by 200 mg/day if a >2g/dL decrease in hemoglobin is observed during any 4 week period. If the patient continues to have hemoglobin levels >12g/dL after Ribavirin dosage reduction, both PEG-Intron and Ribavirin should be permanently discontinued.

**If indirect bilirubin is >5 mg/dl, stop Ribavirin alone for 1-2 weeks. If the indirect bilirubin then decreases to <2.5mg/dL. Ribavirin can be restarted at the reduced dose (decrease dose by 200 mg/day). If the indirect bilirubin remains >4 mg/dl for 4 weeks, both PEG-Intron and Ribavirin are permanently discontinued.

E. At the end of treatment or if treatment is discontinued and PEG-Intron is to be returned to Pharmacy Services for credit, complete the Return and Request for Credit Form (Attachment 15). Instructions for use are on the form.

XI. REASONS TO DISCONTINUE THERAPY

- A. If a new tattoo appears or tattooing equipment is found.
- B. If positive drug screen is reported.
- C. If blood alcohol test is positive.
- D. For Genotype 1:
 1. ALT still elevated at beginning of 4th month.
 2. Hep C Quantasure Plus reveals less than a 2-log reduction from initial value at beginning of 4th month.
 3. Hep C Quantasure Plus remains positive at 6 months.

X. WORK ASSIGNMENTS

Those who test positive for HCV have no work restrictions.

XI. NOTIFYING CHIEF PHYSICIAN AND/OR OFFICE OF HEALTH SERVICES

- A. When treatment is complete.
- B. When treatment is discontinued and why.

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