North Carolina Department Of Safety
Prisons

SECTION: Clinical Practice Guidelines

POLICY # CP-7

SUBJECT: Hepatitis C

EFFECTIVE DATE: October 2015
SUPERCEDES DATE: June 2013

PURPOSE

To provide guidance to primary care physicians in the Division of Prisons Health Services on how to appropriately manage Hepatitis C.

POLICY

DOP Primary Care Providers are expected to follow this guideline except when in their professional judgment on a case-by-case basis there is reason to deviate from these guidelines. If a deviation is made the PCP will document in the medical record any deviations from this guideline and the reasoning behind the need for any deviation.

Natural History of Chronic HCV Infection

Most persons infected with HCV develop chronic infection; however, small subset of newly infected persons is able to clear the virus spontaneously. Chronic HCV infection frequently results in high levels of HCV RNA in the blood, ranging from 10^5 to 10^7 international units (IU)/mL, despite the presence of HCV antibodies. The majority of persons with chronic HCV infection are asymptomatic. Chronic HCV infection has an unpredictable course, frequently characterized by fluctuations in ALT levels that may or may not be associated with significant liver disease. Approximately one-third of persons with chronic HCV infection have no laboratory or biopsy evidence of liver disease.

A small, but significant subset of persons with chronic HCV infection develop progressive fibrosis of the liver that leads to cirrhosis. Transfusion-acquired HCV, high levels of alcohol consumption, older age at the time of infection, HIV infection, chronic HBV infection, the presence of HCV genotype 3, and male gender are associated with an increased risk of disease progression. However, the degree of viremia ("viral load") does not affect the progression of liver disease. Other factors that appear to increase the risk of cirrhosis, and decrease the response to antiviral therapy, include: hepatic steatosis, marked necroinflammation on biopsy, and certain host immunologic characteristics. Once cirrhosis develops in persons with chronic HCV infection, the risk of hepatocellular carcinoma (HCC) is about 1–4% per year. HCV accounts for one-third of the cases of HCC in the U.S. each year.

PROCEDURE

Stepwise Approach for Detecting, Evaluating, and Treating Chronic Hepatitis C

The North Carolina Department of Public Safety, Adult Correction Division/Health Services Section has adopted the stepwise approach previously used by the Federal Bureau of Prisons to detect, evaluate, and treat Hepatitis C.

Following **Table 1**, the policy will outline the components that are to be addressed at each step in the process. Although, this stepwise approached has been adopted, the judgment of the clinician remains the hallmark for appropriate care and management in all cases of Hepatitis C. Any deviation from this approach, however, must be clearly documented in the patient record and such documentation should reflect the reasoning for deviation.

Table 1

Steps for Detecting, Evaluating, and Treating Chronic Hepatitis C

Step 1. Appropriately screen inmates for hepatitis C.
Step 2. Provide initial medical follow-up for anti-HCV positive inmates. All anti-HCV positive inmates should be counseled about:
- the natural history of HCV
- risks of transmission to others
- lifestyle changes that can minimize disease progression.

Step 3. Conduct a pre-treatment evaluation for all inmates who are HCV positive
Step 4a. Determine if hepatitis C treatment is *contraindicated.*
Step 4b. Monitor HCV-infected inmates who are *not* on treatment.

For inmates who may be eligible for hepatitis C treatment, proceed as follows:
Step 5. Obtain HCV genotype, Quantitative HCV RNA viral load, and Fibrosure
Step 6. Determine if treatment should be initiated or not and obtain Informed Consent if treatment indicated.
Step 7. Initiate UR and refer to Hepatology Clinic.

Components for each step:

Step 1.

Appropriately screen for Hepatitis C.
Discuss risk factors and if present, consider testing for Hepatitis C. If testing for Hepatitis C is indicated, HCVab (anti-HCV) should be ordered.

Presence of following increases risk for Hepatitis C:

- ☐ Chronic hemodialysis or ever received hemodialysis
- ☐ Elevated ALT levels of unknown etiology
- ☐ Evidence of extrahepatic manifestations of HCV (mixed cryoglobulinemia, mebranoproliferative glomerulonephritis, or porphyria cutanea tarda)
- ☐ Ever injected illegal drugs or shared equipment
- ☐ Received tattoos or body piercings **while in jail or prison**
- ☐ HIV-infected or chronic HBV infection
- ☐ Received a blood transfusion or organ transplant before 1992, or received clotting factor transfusion prior to 1987
- ☐ History of percutaneous exposure to blood

Step 2.

Provide initial medical follow-up for anti-HCV positive inmates.

- ☐ **Take a medical history and perform a physical examination.**
- ☐ **Try to establish duration of HCV infection by history (e.g., time period of injection drug use)**
- ☐ **Obtain baseline labs**

HIV
HBsAb, HBsAg, HBcAb*
Anti HAV(IgG)
CBC with diff
ALT, AST
TSH, T4
Bilirubin, Alk Phos
Albumin
INR
Creatinine

Ferritin, Iron Saturation
ANA (Further w/u of other liver diseases such as Wilson disease, hemochromatosis, etc may be considered if clinically warranted)

* HBsAg to determine current infection and HBcAb to determine if prior exposure; Anti-HBs to determine immunity.

- ☐ Evaluate inmate for other potential causes of liver disease.
- ☐ Initiate patient counseling
- ☐ Initiate preventive health measures listed below:

  • **Hepatitis B vaccine:** Indicated for inmates with chronic HCV infection. For foreign-born inmates, consider prescreening for hepatitis B immunity prior to vaccination. *Inmates with evidence of liver disease should be priority candidates for hepatitis B vaccination.*
  • **Hepatitis A vaccine:** Indicated for inmates with chronic HCV infection who have other evidence of liver disease. For foreign-born inmates, consider prescreening for hepatitis A immunity prior to vaccination.
  • **Pneumococcal vaccine:** Offer to all HCV-infected inmates with cirrhosis.
  • **Influenza vaccine:** Offer to all HCV-infected inmates annually. Inmates with cirrhosis are high priority for influenza vaccine.

Step 3.
Conduct a pre-treatment evaluation.
Ensure that all recommended pre-treatment evaluations have been completed

- ☐ **Laboratory tests**: Review results of lab tests in previous step.
- ☐ **Pregnancy:** All female inmates of childbearing potential must have a pregnancy test immediately prior to initiating therapy, and monthly thereafter. Continue with monthly tests until 6 months after treatment is completed.
- ☐ **Review** the pros and cons of initiating Hepatitis C treatment with the patient and determine if patient is willing to be treated and adhere to treatment requirements.

If Patient has evidence of Cirrhosis:
• Screen for hepatocellular carcinoma (HCC): If cirrhosis has been diagnosed, regular surveillance with hepatic ultrasound and AFP approximately every 6months should be initiated. (Reference AASLD guidelines)

- Screen for esophageal varices: Consider an upper endoscopy for any inmate with known cirrhosis and evidence of portal HTN

Step 4a.
Determine if Hepatitis C treatment is contraindicated

(1) Inmate will be incarcerated for an insufficient period of time to complete treatment. Usually a twelve (12) month period would be required to complete assessment and treatment for Hepatitis C.
(2) Inmate has an unstable medical or mental health condition which precludes antiviral therapy.
(3) Inmate refuses treatment.
(4) Inmate life expectancy estimated to be less than 10 years due to co-morbid conditions
(5) Inmate has infractions related to use of alcohol or drugs in the last twelve (12) months

If any one of the above five (5) conditions is present, then **STOP** further treatment-related work-up. No further HCV testing (i.e., HCV RNA, genotype, fibrosure) is indicated at this time. If conditions change, reconsider for Hepatitis C treatment.

Step 4b.
Monitor HCV-infected inmates who are not on treatment.

- ☐ Have a plan for each inmate: Outline the plan clearly in the Progress Notes.
- ☐ Obtain baseline laboratory evaluations as noted in Appendix 1 if not already done..
- ☐ Follow these labs at intervals as noted below:
  - ☐ Every 6 months: ALT, AST, bilirubin, albumin, and INR
  - ☐ Every year: CBC (with differential & platelets).
  - ☐ Other labs as clinically indicated (e.g. HbA1C (diabetics); TSH and free T4 (if hyperthyroid)).

Note: The following tests are generally NOT indicated for inmates <u>not</u> on treatment.

- **HCV RNA and HCV genotype:** These tests are not needed unless treatment is indicated. Do not periodically check HCV RNA values for inmates who are not currently candidates for treatment. There is no correlation between HCV RNA levels and the risk or rate of disease progression.
- **Alpha fetoprotein**: Unless cirrhosis is known or strongly suspected, alpha fetoprotein is unnecessary because the risk for hepatocellular carcinoma in HCV infection does not begin until the development of cirrhosis.

- **Liver ultrasound or CT examinations:** Similarly, do not perform periodic liver ultrasound or CT examinations unless cirrhosis is present or there is another definitive indication.
- **Serum ammonia levels**: In a patient with known liver disease, the serum ammonia level has no prognostic value, nor can it be used for monitoring the effectiveness of medications such as lactulose. Serum ammonia levels are only useful in a delirious patient whose diagnosis is uncertain.

Treatment for hepatitis C will be prioritized based on level of fibrosis, advanced liver disease, and those with highest risk (co-infection with HIV and/or HBV)
For inmates who may be eligible for hepatitis C treatment, proceed as follows.

Step 5.
Obtain HCV RNA assay, HCV genotype and Fibrosure.

Before initiating antiviral therapy, an HCV RNA (viral load) is required in order to confirm chronic infection and guide therapy. If the HCV RNA level is undetectable, the individual can be considered uninfected.

a) Obtain HCV RNA by PCR Quantitative with reflex to genotype
   i) If non-detectable, redraw in three months and at six months, if still undetectable then patient no longer has HCV.
   ii) If positive, proceed with evaluation

The HCV genotype should be ordered in conjunction with the initial HCV RNA test. In general, the test for genotype is not repeated—unless re-infection is suspected.

b) Obtain Fibrosure
   Fibrosure is a non-invasive test measuring liver scarring in Hepatitis C (or B), resulting in scores which correspond to the 0-4 point METAVIR Fibrosis (scarring) scale. FibroSure is the most frequently used serum fibrosis marker and consists of an algorithm of five fibrosis markers (alfa2-macroglobulin [g/l], apolipoproteinA1 [g/l], total bilirubin [micromoles/l], haptoglobin [g/l], Gamma GT [IU/l]).

Fibrosis Scoring:

<0.21 = Stage F0 – No fibrosis
0.21 – 0.27 = Stage F0 – F1
0.27 – 0.31 = Stage F1 – Portal fibrosis
0.31 – 0.48 = Stage F1 – F2

0.48 – 0.58 = Stage F2 – Bridging fibrosis with few septa
0.58 – 0.72 = Stage F3 – Bridging fibrosis with many septa
0.72 – 0.74 = Stage F3 – F4
>0.74 = Stage F4 – Cirrhosis

A Fibrosure score of >0.48 (Stage F2) should be referred for treatment.
If Fibrosure score is <0.48, inmate should be followed and tested annually.

Step 6.
Determine if treatment should be initiated or not and obtain Informed consent if indicated.

The patients who should be referred for possible treatment include:

- **Patients with Fibrosure score of >0.48 (Stage F2)**
- **Patients co-infected with HIV and/or HBV irrespective of Fibrosure**

☐Counsel patient regarding the pros and cons of initiating Hepatitis C treatment
☐Determine if patient is willing to be treated and to adhere to treatment requirements.
☐Document rationale for decisions about treatment in the medical record.

Review with the patient and complete the Informed Consent form for Hepatitis C treatment (Revised DC 475) and initiate further treatment if the patient agrees.

If the patient does not meet the criteria above, continue monitoring the patients as in Step 4b above. Annual Fibrosure testing may be performed.

Step 7
Initiate the UR process for referral to Hepatology Clinic

If the patient meets the above criteria, initiate UR for Hepatology Clinic evaluation.
A UR request indicating that all the steps 1 -6 have been completed should be entered. UR reviewers may request documentation for any of the above steps. Include the result of Fibrosure test in the comments. Once the UR is approved, appointment should be scheduled for Hepatitis C Clinic.

Paula Y. Smith, M.D. 11/1/2015

Paula Y. Smith, MD, Chief of Health Services Date

SOR: Deputy Medical Director

Table 1: *Some drugs that may cause liver damage:

Drugs that may cause ACUTE DOSE-DEPENDENT LIVER DAMAGE (resembling acute viral hepatitis)

- acetaminophen
- salicylates (doses over 2 grams daily)

Drugs that may cause ACUTE DOSE-INDEPENDENT LIVER DAMAGE (resembling acute viral hepatitis)

- acebutolol
- indomethacin
- phenylbutazone
- allopurinol
- isoniazid
- phenytoin
- atenolol
- ketoconazole
- piroxicam
- carbamazepine
- labetalol
- probenecid
- cimetidine
- maprotiline
- pyrazinamide
- dantrolene
- metoprolol
- quinidine
- diclofenac
- mianserin
- quinine
- diltiazem
- naproxen
- ranitidine
- enflurane
- para-aminosalicylic acid
- sulfonamides
- ethambutol
- penicillins
- sulindac
- ethionamide
- phenelzine
- tricyclic antidepressants
- halothane
- phenindione
- valproic acid
- ibuprofen
- phenobarbital
- verapamil

*Refer to Up-to-Date(Online Resource) for more extensive list

North Carolina Division of Prisons Health Services
Hepatitis C Therapy Informed Consent
(adapted from U. S. Department of Justice – Federal Bureau of Prisons)

After discussing each item with the inmate, the health care provider should have the inmate:

- *initial numbers 1 through 4 for all patients being considered for hepatitis C treatment,*
- *numbers 5 through 9 if treatment includes peginterferon,*
- *numbers 10 through 13, if treatment includes ribavirin,*
- *numbers 14 through 20 if treatment includes Harvoni or sofosbuvir,* and
- *numbers 21 through 27 if treatment includes simeprevir.*

I, _____, OPUS No._____, hereby authorize Dr. _____ , or his/her relief (designee), to prescribe treatment of Hepatitis C virus infection (HCV) with medication, if indicated, and to continue said medication as is recommended by DPS Prisons Clinical Practice Guidelines.

1. _____ Your health care provider will prescribe the regimen that is most appropriate for your condition. This regimen may consist of a combination of HCV antivirals that could include: Ledipasvir/Sofosbuvir (Harvoni) , pegylated interferon injections (PEG-Intron®, Pegasys®), oral ribavirin (Rebetol®, Copegus®), oral direct-acting agents sofosbuvir (SovaldiTM), simeprevir (OlysioTM), or other direct acting antiviral therapy. I understand my medical condition and why this combination of medications is being recommended to treat my disease.
2. _____ This treatment requires frequent visits to the Health Services Unit for outpatient visits, blood tests, medication injections and pill line administration of some medications. Attending these appointments and adhering to the treatment regimens are essential to achieve a safe and successful treatment result and to reduce the likelihood of the virus becoming resistant to treatment. Prior to starting treatment, each patient must assess their ability and willingness to comply with the treatment regimen described by their health care provider. In some cases, postponing treatment may be acceptable or even preferred. You may be moved to a different facility for completing this treatment.

3. _____ **It is important to abstain from illicit drug or alcohol use, or from receiving tattoos which may interfere with medication treatments, worsen liver disease, or increase the risk for reinfection with HCV or other infections.**
4. _____ This treatment is associated with numerous adverse and potentially serious side effects. Your health care provider, along with pharmacy and laboratory, will carefully monitor you for side effects and your response to this therapy. **To ensure continuity of care and provide the best opportunity for a successful outcome, a medical hold status that prevents your transfer to another institution and/or defers your halfway house placement may be placed until the course of therapy is complete.**

For patients treated with pegylated interferon, the following applies:
5. _____ The most common side effects are "flu-like" symptoms, such as headache, fatigue, muscle aches, and fever. These symptoms may decrease in severity as treatment continues. Taking acetaminophen (Tylenol®) prior to interferon administration may help alleviate some of these adverse effects.
6. _____ Psychiatric problems, such as insomnia and depression, are frequently associated with this therapy. If you feel you are getting irritable or easily upset, feel hopeless or bad about yourself, or experience any other uncommon psychological problems, you should immediately contact your health care provider. More severe psychiatric problems also may occur, including psychosis, severe depression, suicidal thoughts, or completed suicide.
7. _____ Some patients will develop blood problems such as reduced red blood cells (anemia), or reduced white blood cells or platelets. You will receive a Complete Blood Count on a regular basis to determine if you are developing any of these adverse effects. If these levels drop below acceptable levels the medication may need to be dose adjusted or discontinued.
8. _____ Your thyroid function will be closely monitored because a small percentage of patients (approximately 4%) will develop thyroid dysfunction that may be irreversible, even if treatment is discontinued.
9. _____ Other common side effects include bruising, irritation, or itchiness at the injection site, nasal stuffiness, and reversible thinning of the hair.

For patients treated with ribavirin, the following applies:
10. _____ **Ribavirin can cause birth defects. Both women and men, particularly those awaiting release, must be counseled to use adequate**

birth control (2 forms of birth control) during treatment and 6 months after treatment is completed.

11. _____ **Ribavirin should not be taken if you have severe kidney dysfunction.**

12. _____ Between 5%-10% of the patients taking ribavirin therapy develop anemia within 1 to 4 weeks of beginning treatment. You should immediately speak to your doctor if you experience any side effects, or you experience trouble breathing, chest pain, severe stomach or lower back pain, bloody diarrhea or bloody bowel movements, high fever, bruising, bleeding, decreased vision, weight loss, rashes, or other symptoms that concern you.

13. _____ To improve your comfort and the chances of successfully completing this course of treatment you should get plenty of rest, exercise lightly but regularly, drink plenty of water or clear fluids every day, eat regularly, and take acetaminophen for fevers and "flu-like" symptoms.

If oral direct-acting agents are not a treatment option for this patient, skip to the signature blocks at the bottom of page 2.

For patients treated with the HCV polymerase inhibitor sofosbuvir, the following applies:

14. _____ Sofosbuvir is **indicated for the treatment of HCV genotype 1, 2, 3, or 4, and for HCV/HIV coinfection, and must be taken in combination with other HCV antiviral medications. It should never be taken by itself.**

15. _____ Sofosbuvir must be taken by mouth once daily with or without food.

16. _____ Common side effects include fatigue, headache, nausea, insomnia, and anemia.

17. _____ Sofosbuvir should not be taken or prescribed if you already are taking certain other medications. A comprehensive medication review is essential before initiation of Hepatitis C treatment. Your health care provider will discuss these medications in greater detail. If a new medication is prescribed for you while you are taking an HCV polymerase inhibitor, you should inform them that you are taking these medications.

18. _____ Due to the high potential for development of resistance, if sofosbuvir is discontinued, it shall not be restarted.

For patients treated with the HCV protease inhibitor simeprevir, the following applies:

19. _____ Simeprevir is **indicated for the treatment of HCV genotype 1 only and must be taken in combination with other HCV antiviral medications. It should never be taken by itself.**
20. _____ Simeprevir must be taken by mouth once daily with food. There is no specific requirement for type or amount of food. The capsule must be swallowed whole.
21. _____ If you forget to take a dose of simeprevir and it is less than 12 hours after the usual dosing time, you may take the missed dose with food as soon as possible. If it has been more than 12 hours since the usual dosing time, skip that dose and resume the dosing schedule at the next scheduled dosing time.
22. _____ Simeprevir can be stored at room temperature up to 86oF.
23. _____ Common side effects include photosensitivity and rash.
24. _____ Simeprevir should not be taken or prescribed if you already are taking certain other medications. A comprehensive medication review is essential before initiation of Hepatitis C treatment. Your health care provider will discuss these medications in greater detail. If a new medication is prescribed for you while you are taking an HCV protease inhibitor, you should inform them that you are taking these medications.
25. _____ Due to the high potential for development of resistance, if simeprevir is discontinued, it shall not be restarted.

Physician Signature _____
Based upon interview, assessment, and medical record review, it is my opinion that this patient understands the proposed treatment, the risks and benefits of the treatment, and **is competent** to give consent.

Physician Signature _____
Based upon interview, assessment, and medical record review, it is my opinion that this patient understands the proposed treatment, and **is not competent** to give consent.

Other issues discussed:

_____

_____

I certify that I have read the foregoing, or have had it explained to me in a language that I understand; that I have no additional questions; and that I consent to treatment. I understand that I may stop taking this medication by contacting the physician. However, I understand that discontinuing the medication may result in failure to control the progression of liver disease.

Inmate Signature: _____

OPUS No. _____ Date: _____

Witness Signature: _____ Date: _____

Attending Physician: _____

(Revised DC 475) 09/2015