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Management of Hepatitis C	ACA Standards: 4-4356M, 4-4367		
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Hepatitis C

Infection with the hepatitis C virus (HCV) can result in both acute and chronic hepatitis. Acute HCV typically leads to chronic infection; 50 to 85 percent of cases develop chronic hepatitis. Chronic hepatitis C infection affects approximately 2 % of the population of the US. It is estimated that 16-41 % of adult prison inmates have serologic evidence of HCV infection. Chronic HCV infection is usually slowly progressive and may not result in clinically apparent liver disease in many patients if the infection is acquired later in life.

Approximately 20 to 30 percent of chronically infected individuals develop cirrhosis over a 20- to 30-year period of time. Chronic HCV is the most common cause of chronic liver disease and the most frequent indication for liver transplantation in the United States. Deaths associated with chronic hepatitis C in the United States are more likely to be due to end stage liver disease rather than hepatocellular carcinoma (HCC). However, HCV accounts for approximately one-third of HCC cases in the United States.

There are at least 6 major genotypes. Genotype 1 is the most common genotype found in the United States, followed by genotypes 2 and 3. The predominant risk factor for Hepatitis C is recent or remote injection drug use. Approximately one third of young (aged 18–30 years) IDUs are HCV-infected. Older and former IDUs typically have a much higher prevalence (approximately 70%–90%) of HCV infection, reflecting the increased risk of continued injection drug use.

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Management of Acute Hepatitis C

Identification of patients with acute HCV is uncommon because the acute process is most often asymptomatic. Acute infection rarely causes hepatic failure. If symptoms are present, they usually abate within a few weeks. Symptoms of acute and chronic illness is similar and nonspecific with fatigue (most common), abdominal pain, anorexia, or jaundice. The majority of patients with acute HCV fail to spontaneously clear the virus (75- 85%) and develop chronic HCV. As a general rule, most patients who are destined to spontaneously clear HCV viremia do so within 12 weeks and usually no later than 20 weeks after the onset of symptoms.

Patients who present with risks for recent exposure to HCV (IVDU, sexual contact, or tattooing) should be screened for hepatitis C. Anti-HCV usually become detectable between 8 and 12 weeks after infection and thus significantly lags behind detectable HCV RNA levels. After 12 weeks, more than 90% of patients will have positive anti-HCV and > 97% of persons by 6 months after exposure. In most patients, HCV RNA can be detected in blood within 2 weeks after infection. Therefore both Anti-HCV screening (enzyme immunoassay) and HCV RNA should be drawn in patients who report recent exposure. Anti-HCV should be redrawn again 6 months later and the HCV RNA should be redrawn 8-12 weeks later.

If the high risk behavior occurred < 4 weeks prior to screening and the patient is seropositive with Anti-HCV, then the patient was infected prior to the reported high risk behavior.

Treatment of acute Hepatitis C involves symptomatic care only; along with enrollment in Chronic Liver Disease chronic clinic if the patient fails to spontaneously clear the virus (which would be evidenced by a negative HCV PCR RNA at 6 months after acquisition of acute HCV).

See MSRM 140125-01 (Management of Viral Hepatitis) for additional information regarding acute HCV.

Management of Chronic Hepatitis C

Previously, Hepatitis C treatment was complex and not without significant side effects; particularly regimens that involved Peginterferon and Ribavirin. New direct-acting interferon-free regimens are now the standard of care for the treatment of chronic hepatitis C and offer cure rates better than 90 %. The pace of change is expected to increase rapidly and subsequent regimens will change with each newly approved direct-acting antiviral medication (DAA). Further, non-interferon based treatments are now indicated in those with cirrhosis. In the midst of these rapidly changing treatment regimens, and evolving inclusion/exclusion treatment criteria, it is imperative that comprehensive care, including treatment prioritization be assisted by the Oklahoma Department of Correction Hepatitis C clinical coordinator. If deemed clinically appropriate, the HCV treatment regimen will be guided by the expertise of the outside Hepatology consulting service through the regularly scheduled telemedicine patient case presentations.

The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver related health adverse consequences, including end-stage liver disease and HCC by the achievement of virologic cure as evidenced by a sustained virologic response (SVR). A SVR is defined by the absence of HCV RNA by polymerase chain reaction 12 -24 weeks after stopping treatment.

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Patients must be carefully screened for absolute and relative contraindications to treatment. Treatment is assigned the highest priority for those patients with advanced fibroses (Metavir F3), those with compensated cirrhosis (Metavir F4), HIV co-infected individuals, and patients with severe extrahepatic Hepatitis C manifestations (e.g. cryoglobulinemia, associated renal disease, and certain types of lymphomas). The Oklahoma Department of Corrections Hepatitis C Treatment Protocol allows for the selection of those patients who are most likely to benefit from treatment.

I. Hepatitis C Protocol

The Hepatitis C Management Protocol addresses the diagnosis of Chronic Hepatitis C, the identification of other types of liver disease, the screening process for medical and mental health contraindications, offender educational materials, and treatment guidelines. Further, Chronic HCV guidelines (especially regarding advanced disease) can be found in Chronic Illness Management Guidelines Attachment B (OP- 140137) and Management of Viral Hepatitis (MSRM- 140125-01). Medication treatment will take place at one of the three centers of excellence for Hepatitis C treatment (DCCC, MBCC, or OSP). At any point during evaluation and treatment, an inmate can decline further evaluation or treatment. Following counseling, a “Waiver of Treatment for Hepatitis C” (DOC 140137.6C) will be signed.

A. Step 1 – Diagnosis of Chronic Hepatitis C Infection.

Risk-based screening (based on risk for HCV infection or based on a recognized HCV exposure) has served as the hepatitis C screening strategy within the ODOC.

The American Association for the Study of Liver Disease recommends screening of individuals who are identified to have increased risk factors. The CDC has recommended one time screening of all “baby boomers”, born between the years of 1945 and 1965. Baby boomers are 5 times more likely to have hepatitis C than other adult Americans (CDC, 2012).

1. HCV Antibody test (CPL #4675) can be ordered at the medical provider’s discretion for any of the following indications. The HCV antibody test does not require approval from the Regional Lead Physician.
 - a. To evaluate clinical signs or symptoms of liver disease
 - b. To evaluate elevated liver enzyme tests of otherwise unknown etiology.
 - c. To evaluate patients with known risk factors for HCV infection; including IV drug use, hemodialysis, known Hepatitis B infection, blood transfusion prior to 1992, and tattooing or body piercing during incarceration.
 - d. To document a claim of HCV seropositivity prior to incarceration

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- e. At the request of the inmate, according to clinical judgment of the medical provider, and if at least 1 year have passed since last negative HCV screening.
 - f. Coinfection with HIV. HIV/ HCV coinfection is common (at least 30 %) since both infections share similar routes of transmission. In patients with chronic HCV infection, concomitant HIV infection is associated with higher rates of morbidity and mortality related to end-stage liver disease. All HIV infected persons should be screened for HCV infection using enzyme immunoassays. Those with antibodies to HCV should have quantitative HCV RNA testing. Patients who are found to be HCV seronegative should undergo HCV RNA testing if they have advanced immunosuppression (e.g., CD4 counts < 100 cells/mm³).
2. Confirm diagnosis of HCV following positive antibody with HCV PCR RNA (CPL 4563).
- B. Step 2 - Assess for Medical contraindications to Treatment. Medical contraindications to HCV treatment include: IVDU, intra-nasal drug use, all other forms of illicit drug use, alcohol use, tattooing, body piercing, pregnancy, any poorly controlled or recently diagnosed chronic medical problem, current chemotherapy for malignancy or diagnosis of cancer within the last 2 years (excluding Lymphomas), renal failure, or any decompensated cirrhosis evidenced by: Ascites, Hepatic Encephalopathy, or Jaundice. Those with a history of bleeding varices (although decompensated) may still qualify for HCV treatment as overall mortality can be changed if they have varices treated (EVL).
1. Review chart for any history of Decompensated cirrhosis evidenced by Ascites (ICD-9 789.5), Hepatic Encephalopathy (ICD-9 348.3), or Jaundice (ICD-9 782.4). If the patient has any of these clinical conditions, calculate the Child Pugh Score. If the Child Pugh score is Class A or B refer the patient to the ODOC HCV Clinical Coordinator or the Chief Medical Officer for Chart review regarding indications/contraindications to treatment. If the Child Pugh is Class C, complete the Medical parole/Commutation Clinical Recommendation note and co-sign this note to the ODOC HCV Clinical Coordinator and the Chief Medical Officer.
 2. Exclude concomitant Hepatitis B with HBsAg (Hepatitis B Surface Antigen, CPL: 2739).
 3. Exclude concomitant Hepatocellular Carcinoma with AFP (Alpha-Fetoprotein CPL: 2625) and Right Upper Quadrant Ultra-Sound.

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4. Assess for renal failure (Creatinine > 2.0), any poorly controlled or recently diagnosed chronic medical problem, pregnancy, or malignancy (excluding Lymphomas) as all of these exclude inmates from HCV treatment. Inmates should be clear of cancer for at least 2 years before HCV treatment work-up.
 5. Witnessed Drug Screens (CPL # 3210): The reinfection rate for those reporting ongoing injection after SVR is 5.3 per 100 person-years, suggesting a modest ongoing risk. It is prudent to therefore obtain a witnessed drug screen the same day the inmate requests HCV treatment. Additional random urine drug screens should be completed if there is high suspicion of drug abuse during treatment work-up. If they fail this drug screen they are immediately disqualified from active treatment consideration for a minimum of 1 year. Further, Coding of this illicit drug use should be placed in the patient's problem list using the ICD-9 code 305.91.
 6. Evaluate patients for additional high risk behaviors including alcohol use, body piercing, or tattooing. Ongoing use of illicit drugs and other high risk behaviors should be fully resolved before proceeding with evaluation. Sustained sobriety and absence of high risk behaviors should be observable over time. Sustained sobriety has been described as lasting at least 1 year, and stable sobriety as lasting at least 5 years (Betty Ford Institute Consensus Panel, 2007).
- C. Step 3 – Assess for Medical Indications to Treatment. Complete the offender's history and physical examination.
1. Physical Exam- Although cirrhosis is ultimately a histological diagnosis, several clinical signs and symptoms strongly suggest the presence of cirrhosis. The following is a list in decreasing order of likelihood ratio of cirrhosis: Caput medusa, loss of body/pubic hair, Hepatic Encephalopathy (HE), gynecomastia, Ascites, spider angiomas, palmar erythema, jaundice and scleral icterus, and liver stiffness. Patients presenting with physical examination findings consistent with advanced liver disease can be considered as higher priority even when the APRI score reflects only mild fibrosis.
 2. Extra-hepatic manifestations of HCV are common (38 %) and often reflect a more advanced disease. If these are found in offenders requesting HCV treatment, they could represent a higher priority for treatment. Extra-hepatic manifestations of HCV include: Hematologic diseases such as Thrombocytopenia, cryoglobulinemia and lymphoma, autoimmune disorders such as thyroiditis, renal disease such as membranoproliferative glomerulonephritis, and dermatologic conditions such as Porphyria Cutanea Tarda, Lichen Planus, or Leukocytoclastic Vasculitis.

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3. Calculate the AST/Platelet ratio Index (APRI) from platelet and AST drawn within the last year:

<http://www.hepatitisc.uw.edu/page/clinical-calculators/apri>.

The APRI model was developed as a simple, easily calculated method to predict significant, severe fibrosis or cirrhosis and has been tested in both HCV monoinfected and coinfecting (HCV and HIV) patients. The APRI is calculated using the patient's aspartate aminotransferase (AST) level and platelet count, and the upper limit of normal of aspartate aminotransferase (AST). A meta-analysis of 40 studies found that an APRI cutoff of greater than or equal to 0.7 had an estimated sensitivity of 77% and specificity of 72% for detection of significant hepatic fibrosis (greater than or equal to F2 by METAVIR). A cutoff score of at least 1.0 has an estimated sensitivity of 61% to 76% and specificity of 64% to 72% for detection of severe fibrosis/cirrhosis (F3 to F4 by METAVIR). For detection of cirrhosis, a cutoff score of at least 2.0 was more specific (91%) but less sensitive (46%).

4. In all offenders with $APRI \geq 2$, thrombocytopenia (or pancytopenia), or PE findings consistent with cirrhosis Calculate the Child –Turcotte- Pugh Score.

Modified Child-Turcotte-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Turcotte-Pugh score of 5 to 6 is considered class A (well-compensated disease); 7 to 9 is class B (significant functional compromise); and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two- year patient survival: class A: 100 and 85 percent; class B: 80 and 60 percent; and class C: 45 and 35 percent.

Child-Turcotte-Pugh classification

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/liter)	2 to 3 mg/dL (34.2 to 51.3 micromol/liter)	>3 mg/dL (>51.3 micromol/liter)
Albumin	>3.5 g/dL (35 g/liter)	2.8 to 3.5 g/dL (28 to 35 g/liter)	<2.8 g/dL (<28 g/liter)
Prothrombin time			
Seconds over control	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

D. Step 4- Send Case manager review

1. Send form DOC 1410137.06A entitled "Case manager Review/Medical Treatment Evaluation" to the inmates assigned case manager for completion (fill in offender name and DOC #). Treatment and follow-up for all Genotypes can be expected to take up to 12 months. The case manager review is also assessing the inmate's misconduct history. The inmate may not have misconduct involving drug use/possession for at least the previous 1 year.
2. Patients will require a minimum of 12 months remaining prior to earliest release date; allowing time for screening process (including initial and random urine drug screens), treatment and follow-up.
3. If less than adequate time remains until earliest release/parole date, refer enroll inmate in Chronic Liver Disease chronic clinic.
4. If 12 months remain until earliest release/parole date proceed to step 5.

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E. Step 5 - Consult the Oklahoma Department of Corrections Hepatitis C Clinical Coordinator.

If after all above screening: APRI ≥ 2 (or thrombocytopenia or stigmata of liver disease), no continued drug abuse or Class X write-ups within the year, at least 1 clean UDS, detectable HCV PCR RNA, and at least 12 months remaining on sentence the inmate should be referred to the ODOC Hepatitis C Clinical Coordinator for EHR chart evaluation and further consideration for HCV treatment. If the patient is determined to be appropriate for further treatment consideration, the clinical coordinator will initiate the medical move to a treating facility; if the patient is not already at a treating facility. If the patient is currently at a treating facility, contact the ODOC Hepatitis C Clinical Coordinator for confirmation regarding continued treatment work-up with Hepatology consultation. After reception at a treatment facility, proceed to step 6.

1. Annual APRI calculations in all HCV offenders- In addition to the case by case consideration for HCV treatment as detailed in this protocol; all offenders with an APRI score of ≥ 0.7 will be considered for HCV treatment annually. Once per year, a designated nurse at each facility will calculate the APRI: <http://www.hepatitisc.uw.edu/page/clinical-calculators/apri> and send results of all offenders to the ODOC HCV Clinical Coordinator for HCV treatment prioritization. Because a score of 0.7- 1.0 correlates with only moderate fibrosis (Metavir F2) these offenders will be at a lower priority than those with APRI scores correlated with advanced fibrosis/cirrhosis.

F. Step 6 - Pretreatment Evaluation

1. Verify Steps 1-5 have been completed
2. Treating provider repeat history and physical examination
3. Order lab tests-Hepatitis C differential Diagnosis Panel- in preparation for Hepatology consultation
 - a. CBC (CPL #1000)
 - b. CMP (CPL # 9179)
 - c. HCV Genotype (CPL # 4804)
 - d. HCV PCR RNA (CPL # 4563)- if it has been greater than 1 year since last drawn.
 - e. AFP (CPL # 2625)- if it has been greater than 6 months since last drawn.
 - f. Hepatitis B surface Antigen (CPL # 2739)- if it has been greater than 6 months since last drawn.

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- g. TSH (CPL # 2835) to assess for associated thyroiditis
- h. PT/INR (CPL # 1425)
- i. Urine Toxicology (CPL # 3210) - Random urine drug screen may be used for ongoing substance abuse, and may be repeated at clinician discretion prior to conclusion of treatment decisions.
- j. Pregnancy Test for women of childbearing age (CPL # 1540)
- k. Calculate the Child Pugh Score

I. Step 7- Hepatology Consultation

1. Review patient information with the Hepatologist from outside Hepatology Consulting Service via monthly scheduled Tele-Health clinics. Complete all diagnostic testing (e.g. labs, EGD, biopsy) as directed by the Hepatologist. The Hepatologist may recommend a liver biopsy versus Liver Fibrosis Panel. If Hepatologist recommends biopsy, refer patient to LMH for liver biopsy. Private prisons may consult with other Hepatitis C treatment specialists.
2. If the patient is considered appropriate for treatment based on the hepatology consultation, and absence of contraindications, proceed to step 10.

J. Step 8 - Treatment

1. Treatment will be guided by outside Hepatology service consultants. Private prisons may consult other treatment authorities.

Medications for the treatment of Hepatitis C are being rapidly developed by various pharmaceutical manufacturers. Therefore, choice of medication regimens will be guided by the consulting Hepatologist. DOC treating providers must make themselves familiar with the indications, dosages, and side effects of the medications being prescribed.

2. Monitoring during treatment

- a. Labs during the treatment phase will be directed by the Hepatologist. All laboratory results will be documented in the electronic healthcare record (EHR).
- b. Dose modifications- will be considered in conjunction with outside Hepatology service consultant based on follow-up lab and clinical evaluation

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K. Step 9 - Post treatment follow-up

1. 12 weeks after completion of treatment
 - a. Vitals signs/ Weight
 - b. Physical Examination focused on stigmata of liver disease
 - c. Adverse Events
 - d. Lab - CBC, CMP, Quantitative HCV – RNA (CPL # 4563), (urine pregnancy test for women of childbearing age)
 - e. The Hepatologist may also recommend the HCV RNA (CPL # 4563) be repeated at 6 and 12 months post treatment particularly if the offender was cirrhotic prior to treatment.
2. If the inmate has a positive HCV-RNA at the end of treatment or 12, 24, or 48 weeks after treatment, enroll inmate in Chronic Liver Disease chronic clinic and await further recommendations from Hepatologist.
3. If the inmate had evidence of cirrhosis prior to treatment and cure, he or she must remain in Chronic Liver Disease Chronic Clinic for routine cirrhosis care. However, his or her ICD-9 code of Unspecified viral hepatitis C without hepatic coma (070.70) should be changed to resolved.

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III. Action

The chief medical officer, will be responsible for compliance with this procedure.

Any exceptions to this procedure will require prior written approval from the director. This procedure will be effective as indicated.

Replaced: Medical Services Resource Manual 140137-06 entitled "Management of Hepatitis C" dated January 8, 2016.

Distribution: Medical Services Resource Manual

Referenced Forms	Title	Located
DOC 140137.06 A	"Case Manager Review/Medical Treatment Evaluation"	Attached
DOC 140137.06 B	"Hepatitis C Frequently Asked Questions"	Attached
DOC 140137.06 C	"Waiver of Treatment for Hepatitis C"	Attached