STATE OF MONTANA
DEPARTMENT OF CORRECTIONS
OPERATIONAL PROCEDURE

Procedure No. DOC 4.5.11A	Subject: **HEPATITIS C VIRUS (HCV) TREATMENT**
Chapter 4: FACILITY/PROGRAM SERVICES	Page 1 of 8 and Attachments
Section 5: Clinical Services	Effective Date: 12/23/2016
Medical Director Signature: /s/ Dr. Paul Rees	Revised: 02/11/2022
Clinical Services Division Administrator Signature: /s/ Connie Winner	

I. PURPOSE

The Department's Clinical Services Division, using evidence-based clinical guidance, will provide appropriate monitoring for all Hepatitis C Virus Antibody positive (HCVAB+) / Hepatitis C Viruspositive (HCV+) offenders, and will provide HCV antiviral drug treatment when determined by clinical indication and/or treatment criteria to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.

APPLICABILITY

All secure care facilities Department owned and contracted, as specified in contract.

II. DEFINITIONS

Directly Observed Therapy (DOT)– Medication or other treatment provided directly by clinical servicesstaff that is not appropriate for self-administration.

Direct Acting Antiviral (DAA)- Medications inhibitors of the NS3/4A protease, the NS5A protein, and the NS5B polymerase. NS3/4A protease inhibitors are inhibitors of the NS3/4A serine protease, an enzyme involved in post-translational processing and replication of HCV.

Qualified Health Care Professionals (QHCP) – Physicians, physician assistants, nurses, nurse practitioners, dentists, mental health professionals and others who by virtue of their education, credentials, and experience are permitted by law to evaluate and care for offenders, including contracted or fee-for-service professionals.

Medical Review Panel (MRP) – A panel of qualified health care professionals that is comprised of the Clinical Services Division administrator, Medical Director, at least two additional health care QHCPs (one of whom must be a physician), and the Department managed care RNs, all of whom are designated to review complex health care cases and health care topics relevant to the patient population under the care and custody of the Department of Corrections.

Electronic Health Record (EHR)- digital version of a patient's medical chart. EHRs are real-time, patient-centered records that make information available instantly and securely to authorized users.

Mountain Pacific Quality Health (MPQH) – A federally designated Quality Innovation Network-Quality Improvement Organization (QIN-QIO) providing drug utilization review services to the Clinical Services Division of the Department of Corrections.

III. HVC Treatment Steps

1. **STEP 1. Test for HCV infection with HCV Ab test.**
   -diagnostic evaluation of other conditions;
   -all inmates screened at least once;
   -prenatal testing for each pregnancy;
   -periodic risk-based testing related to potential HCV exposure; and
   -upon inmate request

2. **STEP 2. Evaluate inmates who are HCV Ab positive.**
   a. problem-focused history and physical exam:
      1) lab tests—CBC, PT/INR, liver panel, serum creatinine and eGFR, hepatitis A&B serology (HBsAg,anti-HBs, anti-HBc total), HIV serology, quantitative HCV RNA viral load.
      2) HCV genotype testing is not routinely required in treatment-naïve cases with no decompensated cirrhosis, hepatocellular carcinoma, liver or other solid organ transplant,chronic hepatitis B virus infection (HBV), or HIV infection.
   b. assess for hepatic cirrhosis/compensation—Calculate APRI score if no obvious cirrhosis;Calculate Child-Turcotte-Pugh (CTP) score if cirrhosis is known or suspected.
   c. if HCV RNA is detectable, determine eligibility for treatment, provide patient education and preventive health care for patients with HCV infection and withcirrhosis.

3. **STEP 3. Treat eligible patients with an approved direct-acting antiviral (DAA) regimen.**
   a. pre-treatment interventions:
      1) obtain a pregnancy test prior to starting treatment; and
      2) repeat CBC, PT/INR, liver panel, serum creatinine and eGFR if previous results were obtained more than 6 months ago.
   b. determine the most appropriate DAA regimen, including an assessment for drug-druginteractions:
      1) with the availability of pangenotypic regimens, a simplified approach takes many of the medication selection factors into consideration to get to a treatment decision quickly in certain patients.
      2) following the AASLD/IDSA simplified algorithm, treatment-naïve inmates with HCV infectionmay be approved for treatment with an 8-week course of glecaprevir/pibrentasvir if there are no drug-drug interactions, and the patient does not have any of the following conditions – decompensated cirrhosis, hepatocellular carcinoma, liver or other solid organ transplant,end-stage renal disease with compensated cirrhosis, or co-infection with HBV and/or HIV.
   c. submit Hepatitis C Treatment Algorithm/Nonformulary Request

Worksheet to Managed Care RN for review. If approved, submit for specific DAA medication to MPQH; and

d. begin treatment and appropriate monitoring.

IV. Pre-Authorization Form for HCV/DAA Treatment

1. Once the QHCP determines offender is an appropriate candidate for DAA medication, the QHCP initiates the Hepatitis C Treatment Algorithm/Nonformulary Request Worksheet filling out the appropriate portions of the form such as the Diagnosis, clinical requirements, eligibility criteria and treatment recommendation.

2. A Qualified Health Care Professional (QHCP) will gather additional information from correctional and other staff to determine offender readiness criteria. The QHCP consults with the managed care nurse at *CorMedical@mt.gov.*

3. The managed care nurse reviews the case, in consultation with the medical director as appropriate, to ensure the case establishes the need for DAA medication treatment. If necessary, the managed care nurse poses questions to the chronic care nurse and documents additional information in the EHR.

4. Once final review is complete and treatment is approved, the managed care nurse will forward the information to MPQH for final treatment recommendations.

5. If treatment is denied as a result of not meeting pre-treatment and readiness criteria, an appeal may be presented to MRP. It is the primary care QHCPs responsibility to request the MRP review.

V. MPQH Review

1. MPQH reviews the information submitted and recommends:
    a. drug regimen approval as submitted;
    b. drug regimen approval subject to additional evidence-based clinical requirements; or
    c. alternative treatment recommendations; and
    d. denial with supporting clinical rationale based on current Department of Corrections policy and community standards of care.

2. The managed care nurse communicates the MPQH recommendation to designated facility nursing staff. If MPQH has recommended a drug regimen, the managed care nurse forwards those recommendations to the prescribing QHCP.

3. The prescribing QHCP orders recommended medication.

VI. Testing Criteria and Method

1. Testing for HCV infection is recommended:
    a. as a screening test for all inmates;

b. as part of a diagnostic evaluation of inmates with certain clinical conditions (e.g., elevated liverenzymes of uncertain etiology);
c. prenatal testing for each pregnancy; and
d. periodic risk-based testing related to potential HCV exposure for all inmates who request testing.

2. The preferred screening test for HCV infection is an immunoassay that measures the presence of antibodies to HCV antigens, referred to as HCV Ab **(**"anti-HCV" in the AASLD Guidance). The presence ofthese antibodies only indicates a history of exposure to the HCV virus, but does not distinguish betweenactive and resolved infection.
    a. initial testing with an HCV RNA test is recommended for cases with a known prior positive HCV Ab if they are at risk for reinfection or suspected of reinfection, and if they previously cleared the HCV spontaneously or achieved a sustained virologic response (SVR) with treatment.
3. An "opt-out" strategy of voluntary testing for HCV infection is recommended for all inmates, regardless of sentencing status, including new intakes and those already in population who have notbeen previously tested.
4. An "opt-out" approach involves an informed refusal of testing, rather than informed consent (or "opt in") for testing. After informing a patient of the indications and plan for testing, the particular test is ordered and performed—unless the patient declines it.
5. Testing is considered voluntary and is good clinical practice but is not required by policy or law. Testing is recommended as soon as practical upon intake as well as for inmates already in population who have not been tested previously.

VII. Risk Factors for HCV Infection

1. The AASLD, CDC, and USPSTF recommend risk factor-based and birth cohort screening for HCV infection.The incarcerated population is reported to have higher prevalence rates of HCV than the general population and is considered as a risk factor for which screening is recommended.

    Other well-described risk factors, either for acquiring a new infection or already having HCV infection,which should be considered when recommending HCV testing to inmates, include:

    - has ever injected illegal drugs or shared equipment, including intranasal use of illicit drugs;
    - received tattoos or body piercings while in jail or prison, or from any unregulated source;
    - high-risk sexual activity, especially HIV-infected men who have sex with men;
    - HIV or chronic hepatitis B virus (HBV) infection;

- received a blood transfusion or an organ transplant before 1992, received clotting factor transfusion prior to 1987, or received blood from a donor who later tested positive for HCVinfection;
- history of percutaneous exposure to blood;
- has ever received hemodialysis *[Order alanine aminotransferase (ALT) monthly and HCV Ab semiannually for inmates on chronic hemodialysis);*
- born to a mother who had HCV infection at the time of delivery;
- born between 1945 and 1965; and
- current pregnancy

VIII. Clinical Conditions for Testing

1. HCV testing is recommended for all inmates with the following clinical conditions:
    - a reported history of HCV infection without prior medical records to confirm the diagnosis;
    - cirrhosis;
    - elevated liver enzyme alanine aminotransferase test (ALT) levels of unknown etiology; and
    - evidence of extrahepatic manifestations of HCV – mixed cryoglobulinemia, membranoproliferative glomerulonephritis, porphyria cutanea tarda, vasculitis.

IX. Refusal of Testing

1. It is recommended that inmates who decline testing at the baseline visit, should be counseled about and offered HCV testing during periodic preventive health visits.- Documentation of treatment refusal will be permanently captured in the offender's health record.

X. Evaluation of Inmates Testing Positive for HCV Ab

1. Initial evaluation of HCV Ab positive inmates includes: (a) a baseline history and physical examination and (b) baseline lab tests. The inmate should also (c) be assessed regarding the need for preventive health interventions such as vaccines and screenings for other conditions, as well as (d) counseled with information on HCV infection.

   Ideally, this evaluation is performed in a timely manner after a positive HCV Ab test result is reported and combines the baseline/initial evaluation and the pre-treatment evaluation into one step.

2. A simplified approach is recommended, especially for HCV treatment-naïve cases. These cases may then proceed directly to treatment with an 8-week course of glecaprevir/pibrentasvir if there are no drug-drug interactions, and the patient does not have decompensated cirrhosis, hepatocellular carcinoma, liver or other solid organ transplant, or HBV

and/or HIV coinfection.

3. If cirrhosis is present, *Assess for Hepatic Cirrhosis and Decompensation*, to determine whether the liver disease is compensated or decompensated.

XI. Baseline Evaluation

1. A baseline clinician evaluation should be conducted for all inmates who are HCV Ab positive. At minimum, this evaluation should include the following elements in the problem-focused history andphysical exam:

   - evaluate for signs and symptoms of liver disease, as well as for evidence of HCV sequelae (e.g.cryoglobulinemia, vasculitis);
   - obtain a past medical history to include co-occurring medical / mental health conditions andcurrent medications, as well as other pertinent aspects of the patient's medical history;
   - quantify prior alcohol consumption, and determine risk behaviors for acquiring HCV infection(See the section on risk factors under *Screening Criteria* (above). Attempt to estimate the earliest possible date of infection, including when risk factors for exposures started and stopped, e.g., the time period in which the inmate engaged in injection drug use;
   - referral for evaluation and treatment of substance use disorder is recommended for inmates with evidence for ongoing high-risk behaviors related to drug and alcohol use, e.g.,incident reports and sanctions related to drug use during their incarceration; and
   - require about prior treatment for HCV infection, specific medications used, dosages anddurationof treatment and outcomes, if known.

2. Offenders receiving treatment prior to and upon entry to a secure facility or community corrections facility will not have the treatment interrupted unless the physician believes that continuing treatment is not in the offender's best interest. If there is reason to suspect the offender has not been compliant with medication immediately prior to entry (e.g., discontinued while in jail), or if the offender engaged in high-risk activities prior to entry, the continuation should be discussed with the offender's community physician andDepartment medical director.

XII. Laboratory Tests

1. Complete blood count (CBC); prothrombin time (PT) with International Normalization Ratio(INR); comprehensive metabolic panel (CMP).
   a. CMP includes liver panel (albumin, total and direct bilirubin, serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and alkaline phosphatase);serum creatinine and calculated glomerular filtration

rate (GFR); and

b. unexplained abnormalities should prompt additional diagnostic evaluations, as clinically indicated, to determine the underlying cause, e.g., low hemoglobin/platelet count or GFR.

2. Serology for hepatitis A (anti-HAV total), hepatitis B (HBsAg, anti-HBs, and anti-HBc total), and HIV (anti-HIV).

    a. refer to the relevant DOC Clinical Guidance for management of a positive HBsAg or HIV test. These tests may need to be repeated prior to starting HCV treatment if risk factors for transmission have occurred since their last test.

3. Quantitative HCV RNA viral load testing, sensitive to ≤ 25 IU/ml, to determine if the inmate has active HCV infection.

    a. undetectable levels of HCV RNA indicate resolved infection or a false positive HCV Ab test. Such cases **do not** require ongoing follow-up or monitoring in a chronic care clinic.

4. HCV genotype testing is no longer routinely recommended for HCV treatment-naïve cases because many of them will be eligible for a pangenotypic regimen.

    a. a genotype does need to be obtained when considering SOF/VEL in a patient with cirrhosis as well as in situations where a non-pangenotypic regimen may be required, including: prior HCV treatment failures, decompensated cirrhosis, hepatocellular carcinoma, liver or other solid organ transplant, HBV and/or HIV coinfection, or drug-drug interactions.

5. Consider other possible causes of liver disease, especially alcoholism, nonalcoholic steatohepatitis (NASH), iron overload, and autoimmune hepatitis, as clinically indicated. Unless otherwise clinically indicated, testing for other causes of liver disease—e.g., antinuclear antibody (ANA), ferritin, iron saturation, ceruloplasmin—are not routinely ordered in the evaluation of a positive HCV Ab test.

    a. a urine drug screen is recommended only if ongoing substance use is suspected or if it is otherwise clinically indicated.

XIII. Preventive Health Measures

1. All inmates who are HCV Ab positive should be evaluated to assess the need for the preventive health interventions. Patients with liver disease should receive standard immunizations that are applicable to an otherwise healthy population, including the following:

    hepatitis B vaccine: Indicated for susceptible 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 susceptible inmates with chronic HCV; and

    influenza vaccine: Offer to all HCV-infected inmates annually.

(Inmates with cirrhosis are highpriority for influenza vaccine.*)*

2. Pneumococcal vaccine: Recommended by the CDC's Advisory Committee on Immunization Practices (ACIP) for use in adults with chronic liver disease, including cirrhosis, regardless of age.Evidence for its use in chronic HCV infection without cirrhosis is limited.

XIV. Patient Education

1. Inmates diagnosed with chronic HCV infection should be counseled by a Qualified Health Care Professional regarding the natural history of the infection, potential treatment options, and specific measures to prevent transmitting HCV infection to others, both during incarceration and on release.

XV. Assessing for Advanced Hepatic Fibrosis and Cirrhosis

1. Assessment is recommended for all inmates with HCV infection in order to select the most appropriatetreatment regimen, prioritize inmates for treatment of HCV, and determine the need for additional health care interventions. Cirrhosis may be diagnosed in several ways:
2. Symptoms and signs that support the diagnosis of cirrhosis may include: Low albumin or platelets, elevated bilirubin or INR, ascites, esophageal varices, and hepatic encephalopathy. However, isolated lab abnormalities may require additional diagnostic evaluation to determinethe etiology.
3. The AST-Platelet Ratio Index (APRI) is the DOC-preferred method for non-invasive assessmentof hepatic fibrosis and cirrhosis.
    a. the APRI score, a calculation based on results from two blood tests—the AST (aspartate aminotransferase) and the platelet count—is a less invasive and less expensive means ofassessing fibrosis than a liver biopsy.
    b. the formula for calculating the APRI score is**:**

[(AST/AST ULN) x 100] / platelet count (10^9/L)

*****A calculator is available at: *http://www.hepatitisc.uw.edu/page/clinical-calculators/apri*

    c. **APRI score ≥ 2.0 may be used to predict the presence of cirrhosis.** At this cutoff, the APRI score has a sensitivity of 48%, but a specificity of 94%, for predicting cirrhosis. Inmateswith an APRI score ≥ 2.0 should have an abdominal ultrasound performed to identify other findings consistent with cirrhosis (see *abdominal imaging studies* bullet below in this list).

d. lower APRI scores have different sensitivities and specificities for cirrhosis. For example, an
APRI score ≥ 1 has a sensitivity of 77% and a specificity of 75% for predicting cirrhosis.

e. the APRI may also be used to predict the presence of significant fibrosis (stages 2 to 4, outof 4). Using a cutoff of ≥ 0.7, the sensitivity is 77% and

specificity is 72% for significant fibrosis.

f. the APRI score may be invalidated in cases of splenectomy. An alternative non-invasive test(e.g., Fibrosure) may be appropriate. If a person is known to have cirrhosis, the APRI is irrelevant and unnecessary.

4. Liver biopsy is not required unless otherwise clinically indicated or if there is uncertainty about the stage of fibrosis, based on results from non-invasive testing or other clinical indicators. However, the presence of cirrhosis on a prior liver biopsy may be used to meet the DOC criteriafor HCV treatment.

5. Abdominal ultrasound is routinely performed in cases of known or suspected cirrhosis, and as clinically indicated on a case-by-case basis. Abdominal imaging studies such as ultrasound orCT scan may identify findings consistent with or suggestive of the following:

   a. cirrhosis (nodular contour of the liver),
   b. portal hypertension (ascites, splenomegaly, varices), or
   c. hepatocellular carcinoma

XVI. Assessing Hepatic Compensation

1. Assessing hepatic compensation is important for determining the most appropriate HCV treatment regimen to be used. The recommended HCV treatment regimen may differ depending on whether thecirrhosis is compensated or decompensated.

   a. the CTP score is a useful tool to help determine the severity of cirrhosis and in distinguishing between compensated and decompensated liver disease in patients with known or suspected cirrhosis. However, if the CTP score indicates compensated cirrhosis but the overall clinical picture issuggestive of decompensated cirrhosis, it may be more appropriate to choose a DAA regimen for decompensated cirrhosis; and

➔ CTP calculators are readily available on the Internet and are not reproduced in this document.

See http://www.hepatitisc.uw.edu/page/clinical-calculators/ctp.

   b. the CTP score includes five parameters (albumin, bilirubin, INR, ascites, and hepatic encephalopathy), each of which is given a score of 1, 2, or 3. The sum of the five scores is the CTPscore, which is classified as shown in the following Table 1:

TABLE 1. USING CTP SCORES TO ASSESS HEPATIC COMPENSATION

CTP SCORE	CTP CLASS	HEPATIC COMPENSATION
5–6	**Class A**	**Compensated cirrhosis**
7–9	**Class B**	**Decompensated cirrhosis**
≥ 10	**Class C**	

- Warfarin anticoagulation will invalidate CTP calculations if the INR is 1.7 or higher.
- It is recommended that cases of decompensated cirrhosis be managed in consultation with a clinician experienced in the treatment of this condition.
- Inmates with CTP Class C decompensated cirrhosis may have a reduced life expectancy and should be considered for Reduction in Sentence/Compassionate Release in accordance with current policy and procedures.

XVII. Additional Interventions for Inmates with Cirrhosis

1. The following recommendations apply to all inmates with cirrhosis, whether they have ongoing or resolved HCV infection;
   a. pneumococcal vaccine: Offer to all inmates with cirrhosis.
   b. hepatocellular carcinoma screening: Liver ultrasound is recommended every 6 months forpatients with cirrhosis.
   c. esophageal varices screening: Screening for esophageal and gastric varices with esophagogastroduodenoscopy (EGD) is recommended for patients diagnosed with cirrhosis.
2. Other healthcare interventions recommended for patients with cirrhosis may include:
   a. nonselective beta blockers for prevention of variceal bleeding in patients with esophagealvarices;
   b. antibiotic prophylaxis if risk factors are present for spontaneous bacterial peritonitis;
   c. optimized diuretic therapy for ascites; and
   d. lactulose and rifaximin therapy for encephalopathy
3. In general, NSAIDs should be avoided in advanced liver disease/cirrhosis, and metformin should beavoided in decompensated cirrhosis.

XVIII. Treatment Criteria and Pretreatment Interventions

1. Sustained virologic response (SVR) rates of 90% or higher can be achieved with DAA medication regimens. Eradication of HCV is associated with a number of improved outcomes, including a reduction in the following: liver inflammation and fibrosis, severity of advanced liver disease and its complications,risk of liver cancer and liver-related mortality, need for liver transplantation, and transmission of HCV infection.

XIX. DOC Eligibility Criteria for HCV Treatment

1. All sentenced inmates with HCV infection (detectable HCV RNA) are eligible for consideration of treatment. The AASLD/IDSA guidance now recommends treatment for acute HCV infection, rather than monitoring for spontaneous resolution over 6–12 months.

   Inmates being considered for treatment of HCV infection should:

   a. have no contraindications to, or significant drug interactions with, any component of thetreatment regimen.
   b. not be pregnant, especially for any regimen that would require ribavirin.
   c. pregnant inmates may be considered for treatment on a case-by-case basis using a shared decision-making model considering the lack of data on DAA safety during pregnancyand the risk of transmitting HCV to the baby.

d. have sufficient time remaining on their sentence in the DOC to complete a course of treatment.

e. if the inmate cannot complete the course of treatment prior to discharge, the health care staff responsible for discharge planning will educate the inmate on obtaining continuing resources in the community. If possible continuity of care will be coordinated with those community resources prior to release.

f. inmates with a more urgent need for treatment but insufficient time remaining in DOC custody, may be considered for treatment if they will have access to medications and healthcare QHCPs for continuity of care at the time of release.

g. have a life expectancy greater than 18 months. Consultation with the Department Medical Director is recommended in cases where life expectancy is uncertain.

h. inmates must demonstrate a willingness and an ability to adhere to a rigorous treatment regimen by showing compliance to previous prescribed treatments as well as an understanding of need to comply with DAA regimen.

i. inmates with evidence for ongoing behaviors associated with high risk of HCV transmission (e.g., injection drug use) are not automatically excluded from consideration for HCV treatment.

j. ideally, such decisions are individualized and made in the context of an integrated model of care in which there is assessment and treatment for substance use disorder, or other disorders intersecting with HCV infection.

k. consultation with Mountain Pacific Quality Health, Regional Medical Director, or Central Office Managed Care Registered Nurse is recommended for making treatment decisions about inmates who become reinfected as a result of ongoing high-risk behavior.

2. Certain conditions are at **higher risk for complications or disease** progression and may require more urgent consideration for treatment, as follows:

a. advanced hepatic fibrosis;
   1) APRI $\geq$ 2.0; or
   2) Metavir or Batts/Ludwig stage 3 or 4 on liver biopsy;

b. known or suspected cirrhosis;

c. liver transplant recipients;

d. hepatocellular carcinoma;

e. comorbid medical conditions associated with HCV, including:
   1) cryoglobulinemia with renal disease or vasculitis;
   2) certain types of lymphomas or hematologic malignancies; and

3) porphyria cutanea tarda

f. immunosuppressant medication for a comorbid medical condition:

1) some immunosuppressant medications (e.g., certain chemotherapy agents and tumor necrosis factor inhibitors) may be needed to treat a comorbid medical condition but are not recommended for use when infection is present. Although data are insufficient and current guidelines are inconsistent regarding treatment of HCV infection in this setting, such cases will be considered for prioritized treatment of HCV on an individual basis.

3. Evidence for progressive fibrosis:
   a. stage 2 fibrosis on liver biopsy, if treatment clinically indicated.

4. Comorbid medical conditions associated with more rapid progression of fibrosis:
   a. coinfection with HBV or HIV
   b. comorbid liver diseases [e.g., autoimmune hepatitis, hemochromatosis, fatty infiltration ofthe liver, steatohepatitis (fatty liver disease)]
   c. diabetes mellitus
5. Chronic kidney disease (CKD) with GFR ≤ 59 mL/min per 1.73 m2.
6. Birth cohort 1945–1965.
7. Continuity of care for those already started on treatment, including inmates who are newlyincarcerated in the DOC.

XX. Pre-Treatment Assessment and Interventions

1. A simplified approach combining Steps 2 and 3 (See *Steps*) into a seamless process is recommended for treatment naïve patients without current or prior history of decompensated cirrhosis, hepatocellular carcinoma, liver transplantation, end-stage renal disease (GFR < 30), HIV or HBV coinfection, or pregnancy.

   a. pretreatment assessment is recommended within 6 months of the projected start of treatment if thereis no cirrhosis or within 3 months, if there is compensated cirrhosis; and

   b. many aspects of the pretreatment assessment also are part of the initial evaluation and do not need to be repeated if consideration for treatment is performed within these time frames. This is an efficient way to accomplish the test-evaluate-treat approach and is recommended whenever feasible.

2. Pretreatment assessment and interventions include the following:

   a. laboratory tests including CBC, PT/INR, liver panel, serum creatinine, calculated GFR:

      1) labs do not need to be repeated if obtained within 6 months in patients without cirrhosis orwithin 3 months in patients with

compensated cirrhosis;

2) consider retesting for HBV and HIV if ongoing risk factors since last test result; and

3) a urine drug screen is not required as part of the pretreatment evaluation and is recommended only if ongoing substance use is suspected or if it is otherwise clinicallyindicated.

b. assessment for hepatic cirrhosis and decompensation:

1) calculation of the APRI score using results from the pretreatment labs. (An APRI score is notneeded if there is confirmed cirrhosis.);

2) calculation of current CTP score for inmates with known or suspected cirrhosis; and

3) an abdominal US is recommended within 6 months of starting treatment for patients withcirrhosis.

c. pregnancy testing and education covering the potential risks of DAAs during pregnancy prior toinitiating treatment in all women with childbearing potential

1) ribavirin is contraindicated in pregnancy and in both male and female partners attemptingto become pregnant.

d. assessment for significant drug-drug interactions:

1) resources for assessing drug interactions with DAA regimens include the AASLD HCV guidance, DHHS antiretroviral guidelines, University of Liverpool HEP Drug Interactions and manufacturers' prescribing information for specific drug interactions.

3. Assessment for current/prior medication adherence:

a. review of incident report history for high-risk behaviors (alcohol/drug possession/use;tattooing);

b. for ribavirin containing regimens:

1) pretreatment ECG is recommended for inmates with preexisting coronary heart disease.

2) if anemia is present and host not been previously evaluated, a diagnostic evaluation is recommended prior to starting treatment;

4. Testing for NS5A resistance-associated substitutions (RASs) is not routinely indicated, but isrecommended prior to treatment with the following regimens or situations:

a. elbasvir/grazoprevir for HCV genotype 1a and GFR ≥30. If RASs are present at position 28,30, 31, or 93, a regimen other than EBR/GZR should be used;

b. sofosbuvir/velpatasvir for treatment-naïve HCV genotype 3 with cirrhosis being considered for 12 weeks of treatment. If the Y93H RAS

is present, RBV is added to a 12-week regimen ofSOF/VEL;

c. sofosbuvir/velpatasvir for treatment-experienced HCV genotype 3 and no cirrhosis;

d. NS5A resistance testing may be considered when ledipasvir/sofosbuvir is an option fortreatment-experienced HCV genotype 1a with no cirrhosis or compensated cirrhosis; and

e. NS3/4A resistance testing is no longer routinely recommended.

5. Patient education—including, but not limited to: how to take the medication, the importance ofadherence, monitoring and follow up, and potential medication side effects. When ribavirin is used, specific counseling about the risks and recommendations related to pregnancy should be provided and captured in the patient's medical record.

XXI. Direct Acting Antiviral (DAAs) Treatment Regimens

1. Recommendations for **DAA treatment** regimens continue to evolve, but still depend on several factors:
   a. HCV genotype, except for pangenotypic regimens;
   b. prior HCV treatment history;
   c. compensated vs. decompensated liver disease;
   d. co-occurring medical conditions (HBV or HIV coinfection, hepatocellular carcinoma, chronickidney disease, solid organ transplant);
   e. resistance-associated substitutions (certain clinical scenarios); and
   f. drug-drug interactions

2. Special considerations**:** Certain conditions require special consideration when selecting an HCV treatment regimen, including decompensated cirrhosis, hepatocellular carcinoma, chronic kidney disease and compensated cirrhosis, solid organ transplant recipients, HBV or HIV coinfection, HCVinfection with multiple genotypes, and pregnancy. These special considerations are addressed in Section 8.

   a. cost: The cost of DAA regimens can vary widely. When more than one regimen is appropriate for an individual case, the most cost-effective regimen is recommended, taking into consideration all the factors listed above.

   b. currently, there are three classes of HCV DAAs: NS5A replication complex inhibitors (-asvir), NS5B polymerase inhibitors (-buvir), and NS3/4a HCV protease inhibitors (-previr). These antiviral medications for HCV infection act directly on some part of the virus, usually the replication mechanism.

   c. DAAs cannot be used as monotherapy. They must be used in combination with at least oneother DAA with or without ribavirin, depending on the clinical scenario.

   d. the most commonly recommended regimens are described briefly on the

next three pages.

Regimens not recommended

- **Monotherapy** with peginterferon, ribavirin, or any of the DAAs.
- **Dual therapy** with peginterferon and ribavirin.
- **NS3/4 HCV protease inhibitors** (boceprevir, simeprevir, or telaprevir)
- **HCV protease inhibitors for genotypes 2, 3, 5, or 6** (paritaprevir, simeprevir)

XXII. Preferred Treatment Regimen

1. For eligible treatment- naïve cases, an 8-week course of glecaprevir/pibrentasvir is recommended, regardless of HCV genotype. Cases not eligible for this short-course, pagenotypic regimen, will need to have a genotype test if not previously performed and selection of one of the other AASLD/IDSA preferred treatment regimens.
2. Alternative treatment regimens: The AASLD/IDSA guidance includes recommendations for some regimens that are not specifically FDA-approved and also describe alternative treatment regimens for situations in which a preferred regimen is not an option. These alternative regimens are not included in this DOC guidance but can be considered on a case-by-case basis.
3. Submit a Hepatitis C Treatment Algorithm/Nonformulary Request with the necessary supporting documentation. If approved, submit non-formulary requests for the specific DAA medications.

➔ *More detailed information about the regimens and the individual medications—including indications and drug interactions—may be found in the AASLD guidance (https://www.aasld.org/publications/practice-guidelines), manufacturer's prescribing information, Facts and Comparisons (available in the Bureau of Electronic Medical Records System (BEMR)), University of Liverpool HEP Drug Interactions website (https://www.hep-druginteractions.org/checker), and other validated resources.*

XXIII. Potential drug interactions

1. In addition to the genotype, prior HCV treatment history, and status of hepatic compensation, as noted above, it is essential to review each treatment candidate for potential drug interactions prior to selecting the most appropriate regimen for HCV treatment. Adjustments of the inmate's current medications may be needed prior to starting treatment for HCV. Since information on drug-drug interactions are updated as new information becomes available, medical literature and drug interaction websites should be checked routinely. Useful resources for potential drug interactions include the AASLD/IDSA guidance, the individual manufacturers' prescribing information, University of Liverpool HEP Drug Interactions website, and the DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.

XXIV. On-treatment monitoring

- For regimens containing ribavirin:
  a. a CBC should be drawn 2 weeks after starting therapy, then at 4 weeks, then monthly; morefrequently as clinically indicated. Ribavirin dosage adjustments may be required.
  b. pregnancy testing is required periodically during and after treatment—usually monthlyduring treatment and for 6 months after completion of treatment when women with childbearing potential are treated with ribavirin-containing regimens.

- For regimens containing elbasvir/grazoprevir, more frequent monitoring of ALT is necessary:
  a. for 12-week regimens, a liver panel including ALT should be drawn at 8 weeks, and as clinically indicated. For 16-week regimens, a liver panel including ALT should be drawn at8 weeks and again at 12 weeks.
  b. ALT increases of less than tenfold should be monitored approximately every 2 weeks andconsideration given to discontinuation of treatment if the ALT elevations persist. Early discontinuation of HCV treatment is also recommended if ALT increases by tenfold—or if less than tenfold, but accompanied by symptoms such as weakness, anorexia, nausea, vomiting, or change in stool color, or *signs* including elevations in conjugated bilirubin,alkaline phosphatase, and INR, related to hepatic dysfunction.

- For patients with evidence of chronic HBV infection (i.e., HBsAg positive) who do not meetestablished criteria for antiviral HBV therapy, either monitoring of HBV DNA levels or prophylactic HBV antiviral medication may be considered.
  a. monitoring with quantitative HBV DNA levels is done prior to starting HCV DAA treatment, periodically during DAA treatment (usually every four weeks), and immediately after DAA treatment. Initiate antiviral HBV treatment if the HBV DNA level increases more than 10-foldfrom baseline or above 1,000 IU/ml if it was previously undetectable.
  b. prophylactic HBV antiviral mediation may be initiated prior to or at the same time HCV DAAtreatment is started, and continued for 12 weeks after DAA treatment completion.

XXV. Post-treatment monitoring

- A quantitative HCV RNA viral load assessment is recommended at 12 weeks after completion oftreatment; if HCV is undetectable, it defines a sustained viral response (SVR).
- If the HCV viral load is undetectable at 12 weeks after completion of

treatment, the inmate may be removed from the chronic care clinic for this condition, if he or she has no cirrhosis, complications, orrelated comorbidities, and the HCV infection has been changed to "resolved" in the problem list.

- Recurrent viremia following an SVR may be due to relapse *or* reinfection. To help distinguish between relapse and reinfection in such cases, an HCV genotype, along with subtyping for genotype 1, should be obtained. If the post-SVR genotype is the same as the pre-treatment genotype, it is not possible to distinguish relapse from reinfection. In addition, ask about and educate on HCV risk factors, assess readiness for retreatment, and consider referring for drug education programming and treatment if there is evidence for ongoing substance use.

XXVI. Ongoing monitoring

- Periodic monitoring is recommended for all those with active infection, including HCV treatment failures, relapse of HCV infection or reinfection, and those with chronic HCV infection who are not yet treated.
- For cases without advanced fibrosis, cirrhosis, or complications, annual evaluation is appropriate. This evaluation should include a focused review of systems and patient educationrelevant to HCV, vital signs and a focused physical examination, and lab monitoring (CBC, PT/INR, liver panel, serum creatinine, calculated GFR, and calculation of the APRI score).
- For patients with cirrhosis or significant comorbidities, even in those who achieve SVR after treatment,evaluation is recommended at least every 6 months, and more frequently when clinically indicated.

XXVII. Special Considerations

- HCV Infection with more than one genotype
  a. very little data are available to guide the selection of a DAA regimen when more than one HCV genotypeare present at the same time. In such cases, selection of either a pangenotypic regimen or a regimen that is effective against both of the existing genotypes is appropriate, in consultation with the Department Medical Director and MPQH.
- HBV/HCV Coinfection
  a. in patients coinfected with HBV and HCV, HBV reactivation may occur during or after treatment with HCV DAAs. Testing for HBV infection—including HBsAg, anti-HBs, and anti-HBc total, as well as HBV DNAlevels in those with a reactive HBsAg—is recommended for all patients being considered for treatment of HCV infection.
  b. if criteria for treatment of HBV are met, it is recommended that

HBV treatment be started prior to or at the same time as HCV treatment, and monitored according to HBV treatment guidance.

c. for patients with evidence of chronic HBV infection (i.e., HBsAg positive) who do not meet established criteria for antiviral HBV therapy, either monitoring of HBV DNA levels or prophylactic HBV antiviral medication may be considered.

d. monitoring with quantitative HBV DNA levels is done prior to starting HCV DAA treatment, periodically during DAA treatment (usually every four weeks), and immediately after DAA treatment. Initiate antiviral HBV treatment if the HBV DNA level increases more than 10-foldfrom baseline or above 1,000 IU/ml if it was previously undetectable.

e. prophylactic HBV antiviral medication may be initiated prior to or at the same time HCV DAA treatment is started, and continued for 12 weeks after DAA treatment completion.

f. for isolated anti-HBc total positive cases with negative HBsAg and anti-HBs, monitor ALT atbaseline, at the completion of HCV treatment, and again during post-treatment follow-up.

- HIV Coinfection:

a. currently recommended HCV regimens are equally effective for HCV mono-infection and coinfection with HIV. However, an alternative HCV regimen or an alternative antiretroviral medication regimen maybe necessary due to potential drug interactions between the HCV DAAs and certain antiretrovirals.

➞ *The following are links to tables showing drug interactions between the HIV antiretrovirals and the HCVDirect Acting Antivirals (DAAs):*

See *https://aidsinfo.nih.gov/guidelines/htmltables/1/7363*

See *https://www.hcvguidelines.org/unique-populations/hiv-hcv*

- Decompensated Cirrhosis

a. treatment of HCV patients with decompensated cirrhosis should be managed in consultation with anexperienced clinician/specialist, with treatment requests considered on a case-by-case basis. The regimens and other considerations listed below are for those with a current or prior history of decompensated cirrhosis. Inmates with decompensated cirrhosis and a CTP score ≥ 10 (Class C) may meet reduction in sentence criteria.

➞ *See Table 2. HCV Treatment Recommendation for Decompensated Cirrhosis. Attachment 2*

- Hepatocellular carcinoma

a. the presence of HCC may impact both the timing of HCV treatment

and the choice of DAA treatment regimen. The timing of treatment for HCV relative to the treatment of HCC is an important considerationthat is impacted by the choice of treatment for HCC and the patient's life expectancy, and is recommended to be done in collaboration with the treating oncologist.

1) in the context of HCV infection, HCC usually occurs in the presence of cirrhosis. Whethercirrhosis is compensated or decompensated affects the choice of DAA medication; and
2) the SVR rates are lower for patients with HCC than those who don't have HCC. Therefore, thesecases are not eligible for the shorter 8-week treatment regimens. Additional data is needed to determine whether a longer duration of treatment will achieve a higher SVR rate.

- Transplant Recipients:
  a. consultation with a transplant specialist is recommended before and in conjunction with treatment ofHCV in liver, kidney or other solid organ transplant candidates or recipients. AASLD-recommended HCV DAA regimens for liver or kidney transplant recipients, as well as potential DAA drug interactions with anti-rejection medications, may be found at https://www.hcvguidelines.org/unique-populations

- Chronic kidney disease (CKD):
  a. HCV is independently associated with the development of chronic kidney disease (CKD). Published studies indicate that HCV is associated with 1) a higher risk of developing proteinuria and CKD; 2) a higher risk for progression to end-stage-liver-disease (ESLD); and 3) an increased risk of mortality fordialysis patients.
  b. patients with CKD, HCV and no cirrhosis may be considered for the simplified approach totreatment. Those with cirrhosis are not eligible for the simplified approach.
  c. no dosage or duration adjustment is required for any degree of renal impairment when usingany of the currently recommended DAAs including elbasvir/grazoprevir (genotypes 1 or 4), glecaprevir/pibrentasvir (genotypes 1-6), ledipasvir/sofosbuvir (genotypes 1, 4, 5, or 6), or sofosbuvir/velpatasvir (genotypes 1-6).
  d. ribavirin doses must be decreased with GFRs ≤50. For GFRs 30–50, ribavirin is dosed 200 mg alternating every other day with 400 mg. For GFR < 30, including hemodialysis, the ribavirin doseis 200 mg daily. Consultation with a transplant specialist is recommended prior to and in conjunction with treatment of HCV in kidney transplant candidates or recipients.

- Pregnancy Considerations
  a. the current AASLD/IDSA guidance recommends consideration of treatment of HCV during pregnancy orbreastfeeding on an individual basis only if the benefits outweigh the potential or unknown risks.
     1) Testing for HCV infection is recommended as part of prenatal care for each pregnancy.
     2) Treatment of HCV infection is recommended before becoming pregnant to decrease the risk ofmaternal-infant transmission.
  b. ribavirin is contraindicated during pregnancy:
     1) women with childbearing potential who are being considered for an HCV regimen that includes ribavirin should be counseled on the adverse fetal effects of ribavirin. They should be advised not to become pregnant during treatment with ribavirin—and for 6 months afterthe treatment has ended. They should also be advised that the same risks apply if a male sexpartner is being treated with ribavirin. A negative pregnancy test should be documented before starting treatment with ribavirin, then monthly during treatment and monthly for 6 months after treatment.
     2) men being treated with ribavirin should also be counseled on the adverse fetal effects of ribavirin. They should be advised not to cause pregnancy in their female sex partners during treatment with ribavirin—and for 6 months after the treatment has ended.
  c. HCV RNA testing is recommended prior to initiating treatment in the postpartum period to determine if spontaneous resolution of HCV infection occurred during the pregnancy.

XXVIII. References

1. *AASLD/IDSA. Recommendations for testing, managing, and treating hepatitis C. AASLD/IDSA website.http://www.hcvguidelines.org.*
2. *American Association for the Study of Liver Diseases and Infectious Disease Society of America Hepatitis C Guidance*
3. *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. AIDS infowebsite. https://aidsinfo.nih.gov/guidelines. Updated October 17, 2017.*
4. *Federal Bureau of Prisons, Clinical Guidance, Evaluation and Management of Chronic HCV Infection http://www.bop.gov/resources/healthcaremngmt.jsp*
5. *Centers for Disease Control and Prevention National Center for Infectious Diseases—Hepatitis Branch ttp://www.cdc.gov/ncidod/diseases/hepatitis/*
6. *MELD Score Calculator http://optn.transplant.hrsa.gov/converge/resources/MeldPeldCalculator.asp?index=98*

7. *National Institutes of Health*
National Institute of Diabetes and Digestive and Kidney Diseases http://www.niddk.nih.gov
8. *National Clinicians' Post-Exposure Prophylaxis PEP line: (888) 448-4911*
http://www.nccc.ucsf.edu/
9. *U.S. Department of Veterans Affairs National Hepatitis C Program*
http://www.hepatitis.va.gov/

Glossary of Abbreviations

MEDICATIONS	
DAA	direct acting antiviral medication
DCV	daclatasvir
DSV	dasabuvir
EBR	elbasvir*
GLE	glecaprevir*
GZR	grazoprevir*
LDV	ledipasvir*
OBV	ombitasvir
PTV	paritaprevir
PEG-IFN	pegylated interferon, peginterferon
PI	protease inhibitor
PIB	pibrentasvir*
PrO	paritaprevir/ritonavir/ombitasvir
PrOD	paritaprevir/ritonavir/ombitasvir/dasabuvir
RBV	ribavirin
RBV-LD	ribavirin, low initial dose
SOF	sofosbuvir*
SMV	simeprevir
VEL	velpatasvir*
VOX	voxilaprevir*
* Medications marked with an asterisk (*) are direct acting antiviral medications (DAAs).	
OTHER TERMS	
AASLD	American Association for the Study of Liver Diseases
ALT	alanine aminotransferase
ANA	antinuclear antibody
APRI	AST to Platelet Ratio Index
AST	aspartate aminotransferase
CBC	complete blood count
CTP score	Child-Turcotte-Pugh score
EGD	esophagogastroduodenoscopy
GFR	glomerular filtration rate
HBV	hepatitis B virus
HBsAg	hepatitis B surface antigen
HCC	hepatocellular carcinoma

HCV	hepatitis C virus

Hepatitis C Treatment Algorithm/Nonformulary Request Worksheet
Montana Department of Corrections

Inmate Name:	**AO#:**	**Date Submitted:**
Parole Eligibility Date:	**Weight (lb.)**: (within 90 days of request)	
Prison Discharge Date:		
APRI Score: APRI Date**:**	**HCV Genotype**: 1a 1b 2 3 4 5 6	

CTP Score (if cirrhotic): Date:

POINTS (circle):	**1**	**2**	**3**
Albumin(g/dL):	>3.5	2.8-3.5	<2.8
Bilirubin(mg/dL):	<2	2-3	>3
INR:	<1.7	1.7-2.3	>2.3

Encephalopathy: ☐ none ☐ grade 1-2 ☐ grade 3-4

Ascites: ☐none ☐diuretic ☐responsive ☐refractory

Liver Biopsy Result (amount of fibrosis):

Date Performed: ☐ Not Performed

☐ Portal ☐ Periportal ☐ Bridging ☐ Cirrhosis ☐ None

Note: For regimens with elbasvir/grazoprevir in thetreatment of HCV genotype 1a, an HCV NSSA virologicresistance test is required.

Prior Antiviral Treatment for HCV: ☐ No ☐ Yes If yes, answer the following:

Drug Names and Dosages:

Start Date: Stop Date: Reason stopped:

Prior Treatment Response ☐ SVR ☐ Relapse ☐ Partial Responder ☐ Null Responder

Requested Treatment Regimen (check all that apply):

☐ Ledipasvir/sofosbuvir (Harvoni)

☐ Elbasvir/grazoprevir (Zepatier) ☐ Glecaprevir/pibrentasvir (Mavyret)

☐ Sofosbuvir/velpatasvir (Epclusa) ☐ Sofosbuvir/velpatasvir/voxilaprevir (Vosevi)

☐ Ribavirin ☐ Other_____

Eligibility Criteria:

☐ Inmate has sufficient time remaining on sentence to complete a course of treatment prior to Pre-release, probation, discharge of sentence, and life expectancy >18 mo.

☐ Inmate is willing and able to adhere to a rigorous treatment regimen (no documented non-adherenceto prior therapy, failure to complete pretreatment evaluation process, or unwillingness to commitor consent to HCV treatment).

☐ No contraindications or drug interactions with requested treatment regimen verified through MPQH

☐ No uncontrolled or unstable medical or mental health conditions.

☐ No current pregnancy

Health Services Staff Name / Signature / Date / Institution

Documentation – include copies of the following with the non-formulary request:

☐ CBC, serum creatinine and eGFR, liver panel, INR (dated within 180 days of request)

☐ HCV RNA viral load (reported as IU/ml) (any time prior to treatment)

☐ HCV genotype (any time prior to treatment) if not treatment naïve or a candidate for simplifiedtreatment.

☐ HIV Ab – if positive, include CD4 and HIV viral load (dated within 180 days of request) andcurrent antiretroviral medication regimen

☐ Hepatitis B serology (sAb, sAg, and cAb)- if HBsAg reactive, include eAg, eAb, and HBV DNA viralload

☐ Liver biopsy report (if performed, but not required unless clinically indicated)

☐ If cirrhosis or APRI $\geq$ 2(defined by pathology or clinical findings), include abdominal US or CT

☐ Pregnancy test if woman with child-bearing potential (dated within 90 days of request)

PROCEDURE FOR SUBMITTING HCV TREATMENT REQUEST

- Generate a non-formulary request for Hepatitis C Treatment.
- Include all information and attach all required documentation from above.
- May scan and attach Hepatitis C Treatment non-formulary request.