HEPATITIS C TREATMENT EVALUATION

1. ASSESSMENT FOR FIBROSCAN® OR LIVER BIOPSY
   - If patient has had a FibroScan® or liver biopsy within the preceding 3 years, repeat evaluation of liver fibrosis 3 years after the most recent assessment or if clinically indicated per practitioner.
   - If patient has extrahepatic manifestations of hepatitis C that warrant treatment, a FibroScan® or liver biopsy is not needed – Skip to Step 3
   - If patient has abdominal imaging highly suggestive of cirrhosis, a FibroScan® or liver biopsy is not needed. The IPN will add a diagnosis of “Cirrhosis” to the patient’s problem list – Skip to step 3.
   - If patient has laboratory and clinic exam findings highly suggestive of cirrhosis, a FibroScan® or liver biopsy is not needed. The practitioner will add a diagnosis of “Cirrhosis” to the patient’s problem list – Skip to step 3.

2. INTERPRET FIBROSCAN® OR BIOPSY RESULTS
   - (full review of report and discussion with MD/DO required; copy of report should be sent to PCP)
   - FibroScan® result: _________ kPa = F: _____ Date of FibroScan®: __________
   - Metavir Score: _________ (fibrosis) Date of biopsy: __________
   - If FibroScan reveals F3 fibrosis, the IPN will add a diagnosis of “Advanced fibrosis (F3)” to the patient’s problem list.
   - If FibroScan reveals F4 fibrosis, the IPN will add a diagnosis of “Cirrhosis (F4)” to the patient’s problem list and refer to a practitioner to schedule appropriate follow-up.

3. ASSESS MENTAL HEALTH STATUS
   - Administer PHQ-9 (form DOC 13-481) Score: _____
   - Review PULHES codes to determine severity of mental illness: “S” = _____
     - S1
       - PHQ-9 score ≤ 6: Cleared and proceed to step 4.
       - PHQ-9 score > 6: Refer to mental health lead for baseline assessment, follow-up, and referral to psychiatric prescriber as needed.
       - Cleared for treatment.
     - S2
       - Refer to mental health lead for baseline assessment, follow-up as needed.
       - Referral to psychiatric prescriber by mental health, only if needed.
       - Cleared for treatment.
     - S3 or S4
       - Refer to mental health lead for baseline assessment and plan regularly scheduled follow-up
       - Refer to psychiatric prescriber for baseline assessment and schedule follow-up every 3 months at a minimum
       - Cleared for treatment.
4. ORDER HEP C BASELINE LABS – CMP, fasting iron studies, ferritin, PT/INR, Hepatitis B sAg, Hepatitis B cAb, Hepatitis B sAb, Hepatitis C RT-PCR, HIV Ab, CBC, urine toxicology, and urine pregnancy (females only). (If any test result is outside range in parentheses, refer to Hepatitis C CRC.)

Within 6 months of starting treatment:

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULTS</th>
<th>DATE</th>
<th>TEST</th>
<th>RESULTS</th>
<th>DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creat. (&lt;2.0)</td>
<td></td>
<td></td>
<td>Ferritin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td></td>
<td></td>
<td>Hep B sAg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td></td>
<td></td>
<td>Hep B cAb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T. Bili. (&lt;1.5)</td>
<td></td>
<td></td>
<td>Hep B sAb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR (&gt;30)</td>
<td></td>
<td></td>
<td>HIV Ab (neg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alb. (&gt;3.5)</td>
<td></td>
<td></td>
<td>Hep C RNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron sat. %</td>
<td></td>
<td></td>
<td>PT/INR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hct (&gt;35)</td>
<td></td>
<td></td>
<td>Platelets (&gt;150)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5. ASSESS INFRACTION RECORD

☐ If no history of drug or alcohol infractions within past year, but history of drug or alcohol use: IPN to email referral to facility Substance Abuse Recovery Unit contract manager for priority substance abuse disorder treatment prior to release.

☐ If history of drug or alcohol infractions within past year or suspected ongoing use: IPN to email referral to facility Substance Abuse Recovery Unit contract manager for expedited substance abuse disorder treatment to start ASAP.

6. ASSESSMENT FOR CONTRAINDICATIONS

(If contraindication is present and considering treatment, refer to Hepatitis C CRC.)

☐ Yes, relative or complete contraindications to treatment:
  ☐ Pregnant
  ☐ Decompensated Liver Disease with CTP > 12 or MELD > 20 – see DOC protocol for liver transplant referral
  ☐ Metastatic hepatocellular carcinoma ☐ Life expectancy ≤ 18 months

☐ Yes, contraindications to treatment with ribavirin:
  ☐ Hemoglobinopathy (e.g., sickle cell disease) or thalassemia
  ☐ Severe coronary disease (e.g., history of an MI, CABG, or active angina in past year)
  ☐ Uncontrolled arrhythmia
  ☐ Hemoglobin ≤ 12 g/dL in men or ≤ 11 g/dL in women
  ☐ Creatinine ≥ 2.0 or Creatinine Clearance < 50 mL/minute

☐ Yes, contraindications to treatment with sofosbuvir-containing regimens
  ☐ Creatinine Clearance < 30 mL/minute
  ☐ On amiodarone without alternatives

☐ Yes, contraindications to treatment with glecaprevir or voxilaprevir:
  ☐ Patient is on a strong CYP3A inducer that cannot be held or changed (e.g. rifamycin, carbamazepine/oxcarbazepine, phenytoin, macrolide, azole, glucocorticoid)
  ☐ Decompensated liver disease (CTP Class B/C)

☐ No contraindications – Proceed to Step 8.
7. **ASSESSMENT FOR RELEVANT DRUG-DRUG INTERACTIONS**

Prior to starting a directly-acting antiviral, all of the current medications that a patient is taking should be reviewed for clinically relevant drug-drug. Some, but not all, of the more common interactions are listed below. Please refer to other sources for a more detailed list (e.g., www.Hep-druginteractions.org)

- Glecaprevir/pibrentasvir: Interacts with digoxin, anticonvulsants, dabigatran, atazanavir, darunavir, ritonavir, efavirenz, rifamycins, ethinyl estradiol, and statins.
- Ledipasvir: Interacts with acid reducing agents, anticonvulsants, rifamycins, digoxin, boosted tipranavir, STRIBILD®, and rosuvastatin.
- Sofosbuvir: Commonly interacts with anticonvulsants, rifamycins, amiodarone, and boosted tipranavir.
- Sofosbuvir/velpatasvir/voxilaprevir: Interacts with acid reducing agents, anticonvulsants, and digoxin.
- Velpatasvir: Interacts with acid reducing agents (all proton pump inhibitors or ranitidine > 150 mg daily) and efavirenz.

8. **PRACTITIONER REVIEW**

Review of available documentation regarding adherence, mental health, medical, and medication issues that may seriously compromise treatment outcome after a full history and physical have been completed (DOC 13-456 Hepatitis C Treatment History and Physical may be used). Treatment for Hepatitis C

- is
- is not

**Recommended at this time.**

Additional reasoning should be documented on a PER (DOC 13-435).

9. **DETERMINE TREATMENT PROTOCOL**

- A specific medication is contraindicated (see steps 7 and 8 above):
  - Glecaprevir/pibrentasvir
  - Ledipasvir
  - Ribavirin
  - Treatment naïve
  - Treatment experienced:
    - Relapser
    - Partial responder
    - Null responder
  - Cirrhosis present
    - Compensated (CTP Class A)
    - Decompensated (CTP Class B or C)
10. TREATMENT REGIMEN RECOMMENDATIONS – Use DOC 13-359

- **Genotype 1**
  - Treatment naïve:
    - ≤ F3 or compensated cirrhosis (CTP Class A) without HIV, HBV, or HCC: Glecaprevir/pibrentasvir times 8 weeks
    - Compensated cirrhosis (CTP Class A) living with HIV, HBV, or HCC: Glecaprevir/pibrentasvir or sofosbuvir/velpatasvir times 12 weeks
  - Treatment experienced with interferon + ribavirin:
    - ≤ F3: Glecaprevir/pibrentasvir times 8 weeks
    - Compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir times 12 weeks
  - Treatment experienced with NS3 protease inhibitor (telaprevir, boceprevir, or simeprevir):
    - ≤ F3 or compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir times 12 weeks
  - Treatment experienced with non-NS5A inhibitor (sofosbuvir):
    - Genotype 1a and ≤ F3 or compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks
    - Genotype 1b and ≤ F3 or compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir times 12 weeks
  - Treatment experienced with NS5A inhibitor (excluding glecaprevir/pibrentasvir):
    - ≤ F3 or compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir times 12 weeks
  - Treatment experienced with glecaprevir/pibrentasvir:
    - ≤ F3: Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks
    - Compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir + weight-based ribavirin times 12 weeks
  - Treatment experienced with sofosbuvir/velpatasvir/voxilaprevir:
    - ≤ F3 or compensated cirrhosis (CTP Class A): glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks
  - Decompensated cirrhosis (CTP Class B or C, CTP score ≤ 12 and MELD <20):
    - Ribavirin eligible: Sofosbuvir/velpatasvir + weight-based ribavirin or ledipasvir/sofosbuvir + low initial dose ribavirin times 12 weeks
    - Ribavirin ineligible: Ledipasvir/sofosbuvir or sofosbuvir/velpatasvir times 24 weeks
    - Prior use of sofosbuvir or NS5A inhibitor: Ledipasvir/sofosbuvir + low initial dose ribavirin or sofosbuvir/velpatasvir + weight-based ribavirin times 24 weeks

- **Genotype 2**
  - Treatment naïve:
    - ≤ F3 or compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir times 8 weeks
    - Compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir or sofosbuvir/velpatasvir times 12 weeks

**Treatment Regimen Recommendations** continued on page 5.
Treatment Regimen Recommendations continued from page 4.

- Treatment experienced with interferon + ribavirin:
  - ≤ F3: Glecaprevir/pibrentasvir times 8 weeks
  - Compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir times 12 weeks
  - Compensated cirrhosis (CTP Class A) on acid suppression: Glecaprevir/pibrentasvir times 12 weeks

- Treatment experienced with sofosbuvir and ribavirin with or without compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir times 12 weeks
- Treatment experienced with NS5aA (ledipasvir, velpatasvir, daclatasvir, elbasvir, ombitasvir) with or without compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks
- Treatment experienced with glecaprevir/pibrentasvir with or without compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks or glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks
- Treatment experienced with sofosbuvir/velpatasvir/voxilaprevir with or without compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks or sofosbuvir/velpatasvir/voxilaprevir + weight-based ribavirin times 24 weeks
- Decompensated cirrhosis (CTP Class B or C, CTP score ≤ 12 and MELD <20): Ribavirin eligible: Sofosbuvir/velpatasvir + starting with low-dose ribavirin times 12 weeks
  - Ribavirin ineligible: Sofosbuvir/velpatasvir times 24 weeks
  - Prior use of sofosbuvir or NS5A inhibitor: Sofosbuvir/velpatasvir + weight-based ribavirin times 24 weeks

Genotype 3

- Treatment Naive:
  - ≤ F3: Glecaprevir/pibrentasvir times 8 weeks
  - Compensated cirrhosis (CTP Class A): NS5A testing
    - Y93H not present: Sofosbuvir/velpatasvir times 12 weeks
    - Y93H present or no NS5A test result: Glecaprevir/pibrentasvir times 12 weeks
  - Treatment experienced with pegylated interferon and ribavirin:
    - ≤ F3: NS5A testing
      - Y93H not present: Sofosbuvir/velpatasvir times 12 weeks
      - Y93H present or no NS5A test result: Glecaprevir/pibrentasvir times 16 weeks
  - Treatment experienced with sofosbuvir + ribavirin +/- interferon:
    - ≤ F3 or compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks
  - Treatment experienced with NS5a (ledipasvir, velpatasvir, daclatasvir, elbasvir, ombitasvir) with or without compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks

Treatment Regimen Recommendations continued on page 6.
### Treatment Regimen Recommendations

<table>
<thead>
<tr>
<th>Treatment experienced with glecaprevir/pibrentasvir with or without compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks or glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment experienced with sofosbuvir/velpatasvir/voxilaprevir with or without compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks or sofosbuvir/velpatasvir/voxilaprevir + weight-based ribavirin times 24 weeks</td>
</tr>
<tr>
<td>Decompensated cirrhosis (CTP Class B or C, CTP score ≤ 12 and MELD &lt;20):</td>
</tr>
<tr>
<td>Ribavirin eligible: Sofosbuvir/velpatasvir + weight-based ribavirin times 12 weeks</td>
</tr>
<tr>
<td>Ribavirin ineligible: Sofosbuvir/velpatasvir times 24 weeks</td>
</tr>
<tr>
<td>Prior use of sofosbuvir or NS5A inhibitor: Sofosbuvir/velpatasvir + weight-based ribavirin times 24 weeks</td>
</tr>
</tbody>
</table>

#### Genotype 4

| Treatment naïve: |
| ≤ F3 or compensated cirrhosis (CTP Class A) without HIV, HBV, or HCC: Glecaprevir/pibrentasvir times 8 weeks |
| Compensated cirrhosis (CTP Class A) living with HIV, HBV, or HCC: Glecaprevir/pibrentasvir or sofosbuvir/velpatasvir times 12 weeks |

| Treatment experienced with interferon + ribavirin: |
| ≤ F3: Glecaprevir/pibrentasvir times 8 weeks or sofosbuvir/velpatasvir times 12 weeks |
| Compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir times 12 weeks |
| Treatment experienced with NS5A inhibitor (excluding glecaprevir/pibrentasvir) with or without compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks |
| Treatment experienced with glecaprevir/pibrentasvir: |
| ≤ F3: Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks or glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks |
| Compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks |
| Treatment experienced with sofosbuvir/velpatasvir/voxilaprevir, with or without compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks or sofosbuvir/velpatasvir/voxilaprevir + weight-based ribavirin times 24 weeks |
| Decompensated cirrhosis (CTP Class B or C, CTP score ≤ 12 and MELD <20): |
| Ribavirin eligible: Sofosbuvir/velpatasvir + weight-based ribavirin or ledipasvir/sofosbuvir + low initial dose ribavirin times 12 weeks |
| Ribavirin ineligible: Ledipasvir/sofosbuvir or sofosbuvir/velpatasvir times 24 weeks |
| Prior use of sofosbuvir or NS5A inhibitor: Ledipasvir/sofosbuvir + low initial dose ribavirin times 12 weeks or sofosbuvir/velpatasvir + weight-based ribavirin times 24 weeks |

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State law and/or federal regulations prohibit disclosure of this information without the specific written consent of the person to whom it pertains, or as otherwise permitted by law.
HEPATITIS C TREATMENT EVALUATION

**Treatment Regimen Recommendations** continued from page 6.

<table>
<thead>
<tr>
<th>PROVIDER</th>
<th>DATE/TIME/INIT</th>
</tr>
</thead>
</table>

- **Genotype 5 and 6**
  - Treatment naïve:
    - ≤ F3 or compensated cirrhosis (CTP Class A) without HIV, HBV, or HCC: Glecaprevir/pibrentasvir times 8 weeks
    - Compensated cirrhosis (CTP Class A) living with HIV, HBV, or HCC: Glecaprevir/pibrentasvir or sofosbuvir/velpatasvir times 12 weeks
  - Treatment experienced with interferon and ribavirin:
    - ≤ F3: Glecaprevir/pibrentasvir times 8 weeks
    - Compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir times 12 weeks
  - Treatment experienced with NS5A inhibitor (excluding glecaprevir/pibrentasvir), with or without compensated cirrhosis (CTP Class A): Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks
  - Treatment experienced with glecaprevir/pibrentasvir:
    - ≤ F3: Sofosbuvir/velpatasvir/voxilaprevir times 12 weeks or glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks
    - Compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 16 weeks
  - Treatment experienced with sofosbuvir/velpatasvir/voxilaprevir, with or without compensated cirrhosis (CTP Class A): Glecaprevir/pibrentasvir + sofosbuvir + weight-based ribavirin times 24 weeks
  - Decompensated cirrhosis (CTP Class B or C, CTP score ≤ 12 and MELD <20):
    - Ribavirin eligible: Ledipasvir/sofosbuvir + low initial dose ribavirin or sofosbuvir/velpatasvir + weight-based ribavirin times 12 weeks
    - Ribavirin ineligible: Ledipasvir/sofosbuvir times or sofosbuvir/velpatasvir times 24 weeks
  - Prior use of sofosbuvir or NS5A inhibitor: Ledipasvir/sofosbuvir + low initial dose ribavirin or sofosbuvir/velpatasvir + weight-based ribavirin times 24 weeks
- Treatment recommended by FMD: Restricted to uncomplicated, treatment naïve patients with F0-F2 fibrosis.
- Referred to Hepatitis C Care Review Committee for review.

**11. ADDITIONAL BASELINE EVALUATIONS**

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULTS</th>
<th>DATE</th>
<th>TEST</th>
<th>RESULTS</th>
<th>DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creat. (&lt;2.0)</td>
<td>_________</td>
<td>_________</td>
<td>Urine tox (neg)</td>
<td>_________</td>
<td>_________</td>
</tr>
<tr>
<td>Hct (&gt;35)</td>
<td>_________</td>
<td>_________</td>
<td>Upreg (neg)</td>
<td>_________</td>
<td>_________</td>
</tr>
<tr>
<td>Platelets (&gt;150)</td>
<td>_________</td>
<td>(females only)</td>
<td>_________</td>
<td>_________</td>
<td>_________</td>
</tr>
</tbody>
</table>

☐ EKG if known or suspected cardiac disease and ribavirin will be part of treatment.

Date of exam: ____________