In the last several months, two new medications indicated for the treatment of chronic hepatitis C infection were released. The new medications are **sofosbuvir (Sovaldi™)** and **simeprevir (Olysio™)**. They represent a significant advance in the treatment of hepatitis C, but are very expensive. As such, the Department of Health and Mental Hygiene has developed clinical criteria for appropriate use. MSFC will be implementing the DHMH criteria effective **July 1, 2014**. The DHMH and MSFC expect strict adherence. A copy of the DHMH criteria is attached. By and large, the DHMH Criteria follow the guidelines set forth by the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. **However, there are several key exceptions:**

- A liver biopsy or other accepted test (e.g., FibroSure) demonstrating fibrosis (**Metavir score > 2**) is required before initiating therapy.
- The combination of **sofosbuvir with simeprevir is excluded**.
- **Mandatory virologic testing at 4, 12 and 24 weeks** must be performed with the intent to discontinue treatment if there is inadequate viral response (defined in the DHMH document).
- The prescribing practitioner must specialize in **Gastroenterology or Infectious Disease**.
- The patient must be **substance abuse free for 6 months** prior to treatment (with some exceptions).
- Initial medication approvals will be for 8 weeks of treatment. **Additional medication will be approved only after lab testing is submitted at week 4 (and week 12 for patients in whom regimens extend greater than 12 weeks).**
- Patients with stable depression or mood disorders are **not** systematically prohibited from the use of interferon.
If you wish to prescribe sofosbuvir (Sovaldi™) or simeprevir (Olysio™), please complete the HEPATITIS C THERAPY PRIOR-AUTHORIZATION FORM and PRESCRIPTION and fax it to 410-933-2205. This form will also serve as a prescription that will be forwarded to CVS Caremark Specialty Pharmacy allowing your patient to receive his/her medication. For any questions, please contact Danielle Gerry, M.D. at 410-933-2295 or Patryce Toye, M.D. at 410-933-2204.
HEPATITIS C THERAPY PRIOR-AUTHORIZATION FORM and PRESCRIPTION
Incomplete form will be returned

Please attach copies of the member’s medical history summary, lab and genetic test reports
**Please review our clinical criteria before submitting this form**

Member Information

| Member: __________________________________________ | Date of Birth: _____/_____/______ |
| MA#: ___________________ | MSFC #: _____________________ | Body Weight: ______ kg |
| Current Home Address: __________________________________________ |
| Current Phone #: (_____) _______-________ |

Diagnosis (Attach genotype test results)

- □ Acute Hep C  □ Chronic Hep C  □ Hepatocellular Carcinoma  □ other:________________________________________
- If s/p TRANSPLANT, □ Genotype of pre-transplant liver: __________________
  □ Genotype of post-transplant liver: __________________
- What is member’s HCV genotype (including subtype)?_________________________
- Has a liver biopsy been performed? □ Yes  □ No  □ No cirrhosis  □ Decompensated liver Ds
  Test date: _____/_____/______
  Provide a copy of biopsy results or other fibrosis test (e.g., FibroSure, HepaScore, et.al),
  Specify Metavir grade:_________________  stage:_________________

Hepatitis C Member Characteristics

- This request is for: □ New Therapy  □ Relapser  □ Partial Responder  □ Non-Responder
  □ Compensated cirrhosis (treatment naïve or experienced)  □ No cirrhosis  □ Decompensated liver Ds

Drug Regimen with Strengths/Dosages/Length of Therapy and Treatment Plan

| Sovaldi®: __________________________________________ | Olysio™: ____________________________ |
| Pegylated interferon: ____________________________ | Ribavirin: ____________________________ |
| Other: __________________________________________ |
| Anticipated total treatment duration: ____________________________ |
Adherence with prescribed therapy is a condition for payment for continuation therapy for up to the allowed timeframe for each HCV genotype. The recipient’s Medicaid drug history will be reviewed prior to approval.

Has drug therapy treatment plan been developed and discussed with member □ Yes □ No
Any issues with drug adherence? □ Yes □ No Explain: __________________________
Adherence assessment: __________________________

Laboratory Results

If prescribing Olysio™, Q80K polymorphism testing:

Test date: _______/_______/________ Result: __________________________
Baseline HCV RNA level (within 30 day pre-treatment): ____________ log10 __________ Date:_______/_______/_______
Liver enzyme levels: Baseline ALT/AST: __________________________ Date measured:_____ / ____ / _____
  Baseline platelet: __________________________ Date measured: _____ / ____ / _____
Baseline hemoglobin/hematocrit: __________________________ Date measured: _____ / ____ / _____

Medical History

Does member have HIV/HCV co-infection? □ Yes □ No
Has the member had a solid organ transplant? □ Yes  □ No   Specify transplant date:_______/_______/_______

Does the member have a history of any of the following: □ No to all
  □ anemia       □ autoimmune hepatitis or other autoimmune conditions □ pregnant □ renal d/s □ thrombocytopenia
  □ severe concurrent medical d/s (i.e. AIDS, cancer, significant CAD) □ hemoglobinopathies (i.e. sickle cell, thalassemia)
  □ currently on didanosine □ unstable CVD

Does the member have history of depression or mood disorder? □ Yes □ No
If yes, is the member stable on current medication? □Yes □ No

Does the member have history of Drug/Alcohol Abuse? □ Yes □ No  If yes, is abstinent for last 6 months? □Yes □ No
If no, does the member have significant progression of disease and is currently in drug rehabilitation program? □ Yes □ No

Prior Drug Utilization

List concomitant drugs that might interact with any of the prescribed Hep C drugs: __________________________
List all previous hepatitis C therapies including adverse effects associated with prior therapy and reason for drug failure. If the member is contraindicated or ineligible to receive a portion of a therapy (interferon), please provide a reason: __________________________
  __________________________
If the member’s MSFC and/or Medicaid eligibility changes during therapy and the member is no longer eligible for Medicaid prescription drug assistance, is the physician prepared to enroll the member in other patient assistant drug programs to complete therapy?  □ Yes  □ No

Prescriber’s Information and Attestation

I certify that the information provided is accurate. Supporting documentation is available for State audits.

_______________________________   Prescriber’s Name: _________________________________ Date: _____/____ /____

(Prescriber’s signature)

Practice Specialty: ____________________      NPI:____________________
DEA: _____________

Telephone# (______) – ____________- ___________                     Fax# (_______) - ____________ - ___________

Address: ____________________________________________
____________________________________________

• Medications will be dispensed through Caremark Specialty Pharmacy
• Initial authorizations will be for 8 weeks per the DHMH guidelines to the Medicaid MCOs
• HCV RNA Level at Treatment week 4 will be **REQUIRED** for continued authorization after 8 weeks
• A copy of the **HEPATICIS C THERAPY CONTINUATION AUTHORIZATION FORM and PRESCRIPTION** will be sent to the prescriber’s fax number provided above prior to the renewal date as a reminder
Clinical Criteria for Hepatitis C (HCV) Therapy

**Diagnosis**
- Must have chronic hepatitis C, genotype and sub-genotype specified to determine the length of therapy;
- Liver biopsy or other accepted test demonstrating liver fibrosis corresponding to Metavir score of greater than or equal to 2;
- Consult performed and medication prescribed by a physician specializing in infectious disease or gastroenterology/hepatology.

**Patient Treatment Plan**
- Patient must have a treatment plan developed by the specialist.
- If patient is of childbearing age, she must utilize 2 forms of contraception.

**Drug Therapy**
- Must be in accordance to FDA approved indications.

**Sofosbuvir (Sovaldi™)**

**RECOMMENDED REGIMENS AND TREATMENT DURATION FOR SOFOSBUVIR COMBINATION THERAPY IN HCV**

<table>
<thead>
<tr>
<th>HCV Genotype and Comorbidities</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with genotype 1 or 4 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + peginterferon alfa + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Patients with genotype 2 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Patients with genotype 3 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Patients with HCV/HIV-1 co-infection (genotype 1 or 4) with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + peginterferon alfa + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Patients with genotype 1 HCV and interferon ineligible, with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Patients with hepatocellular carcinoma awaiting liver transplantation</td>
<td>sofosbuvir + ribavirin</td>
<td>48 weeks (or until the time of liver transplantation; whichever occurs first)</td>
</tr>
</tbody>
</table>
**Age Edit:** Adult patients age ≥18 years old

**Quantity Limit:** One 400 mg tablet per day (28 tablets/28 days).

**Length of Authorization:**
Based on HCV subtype, Patient must be treatment naïve to sofosbuvir.

**INITIAL:** 8 weeks

**REFILLS:** Should be reauthorized for additional 8 week period at a time, depending on the treatment plan. The patient must receive refills within one week of completing the previous 28 day supply throughout treatment.

**Monitoring of the Virological Response**:
- Rapid virologic response (RVR): ≥ 2 log reduction in HCV RNA for the baseline or undetectable after 4 weeks of therapy
- Early Virologic response (EVR): undetectable HCV RNA viral load at treatment week 12
- Sustained virologic response (SVR): HCV RNA negative 12 weeks after cessation of therapy

**DISCONTINUATION OF DOSING**
- It is unlikely that patients with inadequate on-treatment virologic response will achieve a sustained virologic response (SVR), therefore discontinuation of treatment is recommended in these patients.

**Treatment Stopping Rules in Any Patient with Inadequate On-Treatment Virologic Response**

<table>
<thead>
<tr>
<th>HCV RNA</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Week 4: &lt; 2 log reduction in HCV RNA from baseline</td>
<td>Discontinue sofosbuvir, peginterferon alfa and ribavirin</td>
</tr>
<tr>
<td>Treatment Week 12: greater than or equal to 25 IU/mL</td>
<td>Discontinue peginterferon alfa, ribavirin, and sofosbuvir (if applicable)</td>
</tr>
<tr>
<td>Treatment Week 24: greater than or equal to 25 IU/mL</td>
<td>Discontinue peginterferon alfa, ribavirin, and sofosbuvir (if applicable)</td>
</tr>
</tbody>
</table>

**A FDA or AASLD recommendation for the discontinuation of treatment has not been released to date. Prescribers are encouraged to monitor HCV RNA to validate adherence to therapy/efficacy of therapy**
Interferon Alfa Ineligible Defined

• Intolerance to interferon alfa;
• Autoimmune hepatitis and other autoimmune disorders;
• Hypersensitivity to peginterferon alfa or any of its components;
• Decompensated hepatic disease;
• Documented history of depression or mood disorder, which are not stable on the current drug regimen;
• Platelet count <75,000/mm³;
• A history of preexisting cardiac disease.

For documented diagnosis of HCV with genotype 1 [Triple therapy] Combination with peginterferon and ribavirin – Approval for 12 weeks

• Approve; OR
• Approve for HCV/HIV-1 co-infection; OR
• Approve for patients with compensated cirrhosis, including those with hepatocellular carcinoma
• Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting sofosbuvir for a 12 week duration

For documented diagnosis of HCV with genotype 1 [Dual therapy] Combination with ribavirin – Approval for 24 weeks

• Patients MUST be interferon ineligible (document reason that patient is interferon ineligible)
• Approve; OR
• Approve for HCV/HIV-1 co-infection; OR
• Approve for patients with compensated cirrhosis, including those with hepatocellular carcinoma
• Must be used in combination with ribavirin therapy

For documented diagnosis of HCV with genotype 2 [Dual therapy] Combination with ribavirin – Approval for 12 weeks

• Approve; OR
• Approve for HCV/HIV-1 co-infection; OR
• Approve for patients with compensated cirrhosis, including those with hepatocellular carcinoma
• Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 12 week duration
For documented diagnosis of HCV with genotype 3 *[Dual therapy]* Combination with ribavirin – Approval for 24 weeks

- Approve; OR
- *Approve* for HCV/HIV-1 co-infection; OR
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 24 week duration

For diagnosis of HCV with genotype 4 *[Triple therapy]* Combination with peginterferon and ribavirin – Approval for 12 weeks

- Approve; OR
- *Approve* for HCV/HIV-1 co-infection; OR
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting sofosbuvir for a 12 week duration

For diagnosis of hepatocellular carcinoma awaiting liver transplantation *[Dual therapy]* Combination with ribavirin – Approval for 48 weeks

- Sofosbuvir efficacy has been established in subjects with HCV genotype 1, 2, 3 or 4 infection, including those with hepatocellular carcinoma meeting Milan criteria and awaiting liver transplantation)
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 48 week duration or until the time of liver transplantation, whichever occurs first.

- Milan criteria defined as:
  - the presence of a tumor 5 cm or less in diameter in subjects with single hepatocellular carcinoma; AND
  - no more than three tumor nodules, each 3 cm or less in diameter, in subjects with multiple tumors; AND
  - no extrahepatic manifestations of the cancer and no evidence of vascular invasion of the tumor

**ADDITIONAL SOFOSBUVIR INFORMATION TO AID IN THE FINAL DECISION**

- Remind all providers that HCV-RNA levels will need to be obtained at treatment week 4 for continuation of treatment
• Approve for 8 weeks of initial therapy to begin with in order to allow time for lab test results to be processed.
• Must have baseline HCV RNA level within 30 days of anticipated treatment start date
• Patient is not receiving concomitant therapy with a hepatitis protease inhibitor (e.g. telaprevir (Incivek), or boceprevir (Victrelis)).
• Sofosbuvir combination treatment with ribavirin or peginterferon alfa/ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin.
• Patient does not have decompensated cirrhosis (which is defined as a Child-Pugh score greater than 6 [class B or C]).
• Patient does not have severe renal impairment (eGFR <30 mL/min/1.73m²) or end stage renal disease (ESRD) requiring hemodialysis.
• The safety and efficacy have not been established in post-liver transplant patients.
• Patient must be 6 months free of substance/alcohol/opioid dependence.
• There is insufficient data to recommend use in patients with HCV genotypes 5 or 6.
• For HIV-1 lab report documenting that patient has HIV-1; AND
  ☐ CD4 count greater than 500 cells/mm³, if patient is not taking antiretroviral therapy; AND
  ☐ CD4 count greater than 200 cells/mm³, if patient is virologically suppressed (e.g. HIV RNA< 200 copies/mL)

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1 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
2 FDA Antiviral Drugs Advisory Committee Meeting, October 25, 2013; Background Package for NDA 204671 sofosbuvir (GS-7977).
3 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
Simeprevir (Olysio™)\textsuperscript{vi,vi}

**Length of Authorization:**

**INITIAL:** 8 weeks for all three agents

**RENEWAL:** Request week 4 labs for renewal (see below). If meet renewal criteria, then reauthorize an additional 4 weeks of therapy with all three agents for a total duration of 12 weeks.

**Refills:** The patient must receive refills within one week of completing the previous supply.

**Quantity Limit:** Simeprevir 150mg should have a quantity limit of 1 tablet per day for a total duration of 12 weeks.

**Approval Criteria:** Approve simeprevir initially for 8 weeks of therapy if ALL of the following are true:

- Prescriber must specialize in infectious disease or gastro-enterology/hepatology
- Diagnosis of hepatitis C virus (HCV) with genotype 1; **AND**
- Patient CANNOT have failed therapy with an oral protease inhibitor indicated for HCV (e.g., Incivek\textsuperscript{®}, Victrelis\textsuperscript{®}, or Olysio); **AND**
- Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting simeprevir; **AND**
- Must be an adult patient age 18 and over; **AND**
- Patient has NOT had liver transplant; **AND**
- Patient is NOT infected with HCV genotype 1a containing the Q80K polymorphism; **AND**
- Patient is NOT co-infected with HCV/HIV

**RENEWAL**

After 8 weeks of therapy, approve simeprevir, peginterferon alfa and ribavirin for an additional 4 weeks of therapy if HCV-RNA shows a minimum 2 log reduction from baseline at treatment week 4

After 8 weeks of therapy, discontinue simeprevir, peginterferon alfa, and ribavirin if HCV-RNA does not show a 2 log or greater reduction from baseline at treatment week 4.

**DISCONTINUATION OF DOSING**

It is unlikely that patients with inadequate on-treatment virologic response will achieve a sustained virologic response (SVR), therefore discontinuation of treatment is recommended in these patients.
**Treatment Stopping Rules in Any Patient with Inadequate On-Treatment Virologic Response**

<table>
<thead>
<tr>
<th>HCV RNA</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Week 4: greater than or equal to 25 IU/ml</td>
<td>Discontinue simeprevir, peginterferon alfa and ribavirin</td>
</tr>
<tr>
<td>Treatment Week 12: greater than or equal to 25 IU/mL</td>
<td>Discontinue peginterferon alfa and ribavirin (treatment with simeprevir is complete at week 12)</td>
</tr>
<tr>
<td>Treatment Week 24: greater than or equal to 25 IU/mL</td>
<td>Discontinue peginterferon alfa and ribavirin</td>
</tr>
</tbody>
</table>

**Additional information to aid in the final decision:**

- Remind all providers that HCV-RNA viral levels will need to be obtained at treatment week 4 for continuation of treatment with simeprevir and week 12 for continuation of treatment with interferon and ribavirin.
- Approve for 8 weeks of initial therapy to begin with in order to allow time for lab test results to be processed.
- Patient must be 6 months free of substance/alcohol/opioid dependence, unless a patient has significant progression of disease state.
- Patient with confirmed diagnosis and history of depression or mood disorder, if stable on current medication than follow triple drug therapy regimen, otherwise use dual drug therapy regimen.

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vi Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.

vi FDA Antiviral Drugs Advisory Committee Meeting, October 25, 2013; Background Package for NDA 204671 sofosbuvir (GS-7977).

vi Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.


### Retreatment Guidelines

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Treatment</th>
<th>Duration of Total Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended Treatment genotype 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients <em>(with previous HCV protease inhibitor therapy)</em> with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + peginterferon alfa + ribavirin</td>
<td>12 to 24 weeks</td>
</tr>
<tr>
<td><strong>Alternative Regimen genotype 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients <em>(interferon eligible) (with or without previous HCV protease inhibitor therapy)</em> with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + peginterferon alfa + ribavirin</td>
<td>12 to 24 weeks</td>
</tr>
<tr>
<td>Patients <em>(interferon ineligible) (with or without previous HCV protease inhibitor therapy)</em> with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Patients <em>(without previous HCV protease inhibitor therapy)</em> with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>simeprevir + peginterferon alfa + ribavirin</td>
<td>12 weeks with 48 weeks of peg per guidelines</td>
</tr>
<tr>
<td><strong>Recommended Treatment genotype 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + ribavirin</td>
<td>12 weeks (patients with cirrhosis may benefit from an extension to 16 weeks of treatment)</td>
</tr>
<tr>
<td><strong>Alternative Regimen genotype 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients <em>(interferon eligible)</em> with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + peginterferon alfa + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td><strong>Recommended Treatment genotype 3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td><strong>Alternative Regimen genotype 3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients <em>(interferon eligible)</em> with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + peginterferon alfa + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td><strong>Recommended treatment genotype 4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients <em>(interferon eligible)</em> with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + peginterferon alfa + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td><strong>Alternative Regimen genotype 4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with or without compensated cirrhosis (including those with hepatocellular carcinoma)</td>
<td>sofosbuvir + ribavirin</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>

**NOT RECOMMENDED (ALL GENOTYPES)**

Telaprevir, boceprevir, or any monotherapy with any agent