# SOVALDI™ (sofosbuvir) AUTHORIZATION REQUIREMENTS

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| P&T Approval Date | 05/14/2014 |
| Effective Date | |

**Background:**
In December 2013 the treatment paradigm of hepatitis C infection changed with the first highly effective, all oral, interferon-free regimens for the treatment of genotypes 2 and 3 hepatitis C infection, as well as providing the improvement of shorter-duration triple therapy with new oral direct acting agents combined with pegylated interferon and ribavirin for the treatment of genotypes 1 and 4 hepatitis C infection. With this latest shift in treatment, the first-generation protease inhibitors, Victrelis® (boceprevir) and Incivek® (telaprevir), are no longer recommended as standard of care for the treatment of hepatitis C genotype 1 infection.

HPSM's coverage criteria for the new direct-acting agents are based on careful consideration of the evidence-based guidance of professional specialty societies and published guidelines. The Infectious Diseases Society of America (IDSA) and American Association for the Study of Liver Diseases (AASLD) have jointly published evidence-based, expert-developed recommendations for hepatitis C management which state the following in regard to the use of the newly approved direct acting agents, Sovaldi and Olysio, for the treatment of genotype 1 hepatitis C infection: "In many instances, however, it may be advisable to delay treatment for some patients with documented early fibrosis stage (F 0-2), because waiting for future highly effective, pangenotypic, direct acting agent combinations in interferon-free regimens may be prudent." In addition, a report issued in February 2014 by the Institute for Clinical and Economic Review (ICER) for the California Technology Assessment Forum (CTAF) recommended that Sovaldi and Olysio be used only for patients with severe hepatitis complications, such as liver cirrhosis.

As part of our commitment to provide affordable health care benefits, Health Plan of San Mateo actively monitors the development of new clinical evidence and availability of new products and may adjust coverage and strategy accordingly. Based on the evidenced-based guidance available as of March 2014 from professional specialty societies and physician subject matter experts, HPSM will provide benefit coverage for Sovaldi and Olysio in cases of genotype 1 hepatitis C infection when there is documented evidence of stage 3 or stage 4 hepatic fibrosis.

Sovaldi is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen. Sovaldi efficacy has been established in subjects with HCV genotype 1, 2, 3 or 4 infection, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection.[1] The following points should be considered when initiating treatment with Sovaldi:[1]

- Monotherapy of Sovaldi is not recommended for treatment of CHC.
- Treatment regimen and duration are dependent on both viral genotype and patient population.
- Treatment response varies based on baseline host and viral factors

Based on results from the Phase 2a COSMOS study, (Combination Of SiMeprevir and sOfosbuvir in HCV genotype 1 infected patientS), the use of Sovaldi in combination with Olysio™ (simeprevir) for 12 weeks is an effective combination antiviral treatment regimen for hepatitis C, genotype 1 infection.[2]

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In addition to adhering to the coverage criteria, the following information must be submitted with a prior authorization request:

- ❒ Hepatitis C virus (HCV) genotype
- ❒ Hepatitis C virus ribonucleic acid (HCV-RNA) level
- ❒ Treatment status, such as:
  - ❒ treatment naïve
  - ❒ null response
  - ❒ partial response, or
  - ❒ relapse
- ❒ Treatment history, including details of when treatment occurred and medications taken
- ❒ Current medical records for hepatitis C assessment and treatment
- ❒ Biopsy results (if performed)
- ❒ Abdominal imaging
- ❒ Hepatocellular carcinoma screening
- ❒ Fibrosis stage
- ❒ Child-Pugh class
- ❒ History of liver transplant
- ❒ Other liver disease
- ❒ Human Immunodeficiency Virus (HIV) coinfection
- ❒ Autoimmune disease
- ❒ Pregnancy status for women of child-bearing age, including whether the member is contemplating pregnancy, is willing to use contraceptives during treatment, and is willing to use contraceptives for the appropriate exclusion period following treatment
- ❒ Laboratory data, including the following:
  - ❒ Liver function tests (LFTs)
  - ❒ Complete blood count (CBC)
  - ❒ Serum creatinine test
  - ❒ Albumin test
  - ❒ International normalized ratio (INR)
- ❒ Mental health clearance
- ❒ Current and historical illicit drug and alcohol use, including documentation of ongoing abstinence or treatment plan
- ❒ Documentation of:
  - ❒ the home/living situation
  - ❒ reliability with follow-up appointments
  - ❒ ability to comply with the treatment regimen
  - ❒ ability to maintain proper nutrition
  - ❒ the adequacy of the patient's support network
- ❒ Up-to-date Cancer screening, per guidelines and when applicable, including:
  - ❒ colon cancer
  - ❒ breast cancer
  - ❒ cervical cancer
  - ❒ chest x-ray, if high risk
- ❒ Tuberculosis screening

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**Coverage Criteria:**

A. For the treatment of chronic hepatitis C genotype 1 infection in peginterferon eligible patients, **Sovaldi in combination with peginterferon alfa and ribavirin** will be approved based on **all** of the following criteria:

1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype infection

**-AND-**

2. Submission of medical records documenting stage 3 or stage 4 hepatic fibrosis including **one** of the following:
    a) Liver biopsy confirming a METAVIR score of F3 or F4, or alternative scoring equivalent*

    **-OR-**

    b) Transient elastography (Fibroscan) score greater than or equal to 9.5 kPa

    **-OR-**

    c) FibroTest (FibroSURE) score of greater than or equal to 0.58

    **-OR-**

    d) APRI score greater than 1.5

    **-OR-**

    e) Radiological imaging consistent with cirrhosis (e.g., evidence of portal hypertension)

    **-OR-**

    f) Physical findings or clinical evidence consistent with cirrhosis as attested by the prescribing physician

**-AND-**

3. Used in combination with peginterferon alfa‡ and ribavirin

**-AND-**

4. Prescribed by **one** of the following:
    a) Hepatologist
    b) Gastroenterologist
    c) Infectious Disease Specialist

**-AND-**

5. **One** of the following:
    a) Patient is not actively participating in illicit substance abuse or alcohol abuse

    **-OR-**

    b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

**-AND-**

6. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 12 weeks.**

B. For the treatment of chronic hepatitis C genotype 1 infection (without decompensation) in peginterferon ineligible patients, **Sovaldi in combination with Olysio (simeprevir)** will be approved based on **all** of the following criteria:

1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 1 infection

**-AND-**

2. Submission of medical records documenting stage 3 or stage 4 hepatic fibrosis including **one** of the following:
    a) Liver biopsy confirming a METAVIR score of F3 or F4, or alternative scoring equivalent*

    **-OR-**

    b) Transient elastography (Fibroscan) score greater than or equal to 9.5 kPa

    **-OR-**

c) FibroTest (FibroSURE) score of greater than or equal to 0.58

**-OR-**

d) APRI score greater than 1.5

**-OR-**

e) Radiological imaging consistent with cirrhosis (e.g., evidence of portal hypertension)

**-OR-**

f) Physical findings or clinical evidence consistent with cirrhosis as attested by the prescribing physician

**-AND-**

3. Patient is ineligible for treatment with peginterferon alfa, defined by at least **one** of the following:
    a) Autoimmune hepatitis or autoimmune disorders (eg, dermatomyositis, immune [idiopathic)] thrombocytopenic purpura, inflammatory bowel disease, interstitial lung disease, interstitial nephritis, polymyositis, psoriasis, rheumatoid arthritis, sarcoidosis, and systemic lupus erythematosus)
    b) Major uncontrolled depressive illness
    c) Suicidal attempt within past year
    d) History of psychosis, schizophrenia, bipolar disorder, schizoaffective disorder, or suicidal ideation
    e) Uncontrolled seizures
    f) Moderate or severe retinopathy
    g) Poorly controlled diabetes
    h) Baseline neutrophil count below 1,500/ μL
    i) Baseline platelet count below 70,000/ μL
    j) Baseline hemoglobin below 10 g/dL
    k) Solid organ transplant (renal, heart, or lung)
    l) Significant ischemic cardiac disease
    m) Untreated thyroid disease
    n) Pregnant or unwilling to comply with adequate contraception
    o) Prior intolerance or hypersensitivity (urticaria, angioedema, bronchoconstriction, anaphylaxis, or Stevens-Johnson syndrome) to interferon therapy
    p) Symptomatic hepatitis C induced cryoglobulinemia

**-AND-**

4. Used in combination with Olysio (simeprevir)

**-AND-**

5. If the genotype is 1a, documentation of NS3 Q80K polymorphism testing

**-AND-**

6. Prescribed by **one** of the following:
    a) Hepatologist
    b) Gastroenterologist
    c) Infectious Disease Specialist

**-AND-**

7. **One** of the following:
    a) Patient is not actively participating in illicit substance abuse or alcohol abuse

**-OR-**

    b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

**-AND-**

8. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 24 weeks.**

C. For the treatment of chronic hepatitis C genotype 1 infection (without decompensation) in peginterferon and Olysio ineligible patients, **Sovaldi in combination with ribavirin** will be approved based on **all** of the following criteria:

1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 1 infection

**-AND-**

2. Submission of medical records documenting stage 3 or stage 4 hepatic fibrosis including **one** of the following:
    a) Liver biopsy confirming a METAVIR score of F3 or F4, or alternative scoring equivalent*

    **-OR-**

    b) Transient elastography (Fibroscan) score greater than or equal to 9.5 kPa

    **-OR-**

    c) FibroTest (FibroSURE) score of greater than or equal to 0.58

    **-OR-**

    d) APRI score greater than 1.5

    **-OR-**

    e) Radiological imaging consistent with cirrhosis (e.g., evidence of portal hypertension)

    **-OR-**

    f) Physical findings or clinical evidence consistent with cirrhosis as attested by the prescribing physician

**-AND-**

3. Patient is ineligible for treatment with peginterferon alfa, defined by at least **one** of the following:
    a) Autoimmune hepatitis or autoimmune disorders (eg, dermatomyositis, immune [idiopathic)] thrombocytopenic purpura, inflammatory bowel disease, interstitial lung disease, interstitial nephritis, polymyositis, psoriasis, rheumatoid arthritis, sarcoidosis, and systemic lupus erythematosus)
    b) Major uncontrolled depressive illness
    c) Suicidal attempt within past year
    d) History of psychosis, schizophrenia, bipolar disorder, schizoaffective disorder, or suicidal ideation
    e) Uncontrolled seizures
    f) Moderate or severe retinopathy
    g) Poorly controlled diabetes
    h) Baseline neutrophil count below 1,500/ μL
    i) Baseline platelet count below 70,000/ μL
    j) Baseline hemoglobin below 10 g/dL
    k) Solid organ transplant (renal, heart, or lung)
    l) Significant ischemic cardiac disease
    m) Untreated thyroid disease
    n) Pregnant or unwilling to comply with adequate contraception
    o) Prior intolerance or hypersensitivity (urticaria, angioedema, bronchoconstriction, anaphylaxis, or Stevens-Johnson syndrome) to interferon therapy
    p) Symptomatic hepatitis C induced cryoglobulinemia

**-AND-**

4. Patient has contraindication to Olysio therapy (Sovaldi plus Olysio combination therapy is the recommended regimen in patients with interferon ineligibility from the AASLD/IDSA treatment guidelines)

**-AND-**

5. Used in combination with ribavirin

**-AND-**

6. Prescribed by **one** of the following:
    a) Hepatologist
    b) Gastroenterologist

c) Infectious Disease Specialist

**-AND-**

7. **One** of the following:
   a) Patient is not actively participating in illicit substance abuse or alcohol abuse

   **-OR-**

   b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

   **-AND-**

8. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 24 weeks.**

D. For the treatment of chronic hepatitis C genotype 2 infection (without decompensation), **Sovaldi in combination with ribavirin** will be approved based on **all** of the following criteria:
   1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 2 infection

      **-AND-**

   2. Submission of medical records documenting evidence of chronic liver disease (at any stage of fibrosis per biopsy, radiology, or physical findings), or in the absence of chronic liver disease, serologic evidence of persistent infection for at least 6 months

      **-AND-**

   3. Used in combination with ribavirin

      **-AND-**

   4. Prescribed by **one** of the following:
      a) Hepatologist
      b) Gastroenterologist
      c) Infectious Disease Specialist

      **-AND-**

   5. **One** of the following:
      a) Patient is not actively participating in illicit substance abuse or alcohol abuse

      **-OR-**

      b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

      **-AND-**

   b. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 12 weeks.**

E. For the treatment of chronic hepatitis C genotype 3 infection in peginterferon eligible patients, **Sovaldi in combination with peginterferon alfa and ribavirin** will be approved based on **all** of the following criteria:
   1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 3 infection

      **-AND-**

   2. Submission of medical records documenting evidence of chronic liver disease (at any stage of fibrosis per biopsy, radiology, or physical findings), or in the absence of chronic liver disease, serologic evidence of persistent infection for at least 6 months

      **-AND-**

   3. Used in combination with peginterferon alfa‡ and ribavirin

      **-AND-**

   4. Prescribed by **one** of the following:

a) Hepatologist
b) Gastroenterologist
c) Infectious Disease Specialist

**-AND-**

5. **One** of the following:
   a) Patient is not actively participating in illicit substance abuse or alcohol abuse

   **-OR-**

   b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

   **-AND-**

c. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 12 weeks.**

F. For the treatment of chronic hepatitis C genotype 3 infection (without decompensation) in peginterferon ineligible patients, **Sovaldi in combination with ribavirin** will be approved based on **all** of the following criteria:
   1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 3 infection

      **-AND-**

   2. Submission of medical records documenting evidence of chronic liver disease (at any stage of fibrosis per biopsy, radiology, or physical findings), or in the absence of chronic liver disease, serologic evidence of persistent infection for at least 6 months

      **-AND-**

   3. Patient is ineligible for treatment with peginterferon alfa, defined by at least **one** of the following:
      a) Autoimmune hepatitis or autoimmune disorders (eg, dermatomyositis, immune [idiopathic)] thrombocytopenic purpura, inflammatory bowel disease, interstitial lung disease, interstitial nephritis, polymyositis, psoriasis, rheumatoid arthritis, sarcoidosis, and systemic lupus erythematosus)
      b) Major uncontrolled depressive illness
      c) Suicidal attempt within past year
      d) History of psychosis, schizophrenia, bipolar disorder, schizoaffective disorder, or suicidal ideation
      e) Uncontrolled seizures
      f) Moderate or severe retinopathy
      g) Poorly controlled diabetes
      h) Baseline neutrophil count below 1,500/ μL
      i) Baseline platelet count below 70,000/ μL
      j) Baseline hemoglobin below 10 g/dL
      k) Solid organ transplant (renal, heart, or lung)
      l) Significant ischemic cardiac disease
      m) Untreated thyroid disease
      n) Pregnant or unwilling to comply with adequate contraception
      o) Prior intolerance or hypersensitivity (urticaria, angioedema, bronchoconstriction, anaphylaxis, or Stevens-Johnson syndrome) to interferon therapy
      p) Symptomatic hepatitis C induced cryoglobulinemia

      **-AND-**

   4. Used in combination with ribavirin

      **-AND-**

   5. Prescribed by **one** of the following:
      a) Hepatologist
      b) Gastroenterologist

c) Infectious Disease Specialist

**-AND-**

6. **One** of the following:
    a) Patient is not actively participating in illicit substance abuse or alcohol abuse

    **-OR-**

    b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

    **-AND-**

7. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 24 weeks.**

G. For the treatment of chronic hepatitis C genotype 4 infection (without decompensation) in peginterferon eligible patients, **Sovaldi in combination with peginterferon alfa and ribavirin** will be approved based on **all** of the following criteria:
    1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 4 infection

    **-AND-**

    2. Submission of medical records documenting evidence of chronic liver disease (at any stage of fibrosis per biopsy, radiology, or physical findings), or in the absence of chronic liver disease, serologic evidence of persistent infection for at least 6 months

    **-AND-**

    3. Used in combination with peginterferon alfa‡ and ribavirin

    **-AND-**

    4. Prescribed by **one** of the following:
        a) Hepatologist
        b) Gastroenterologist
        c) Infectious Disease Specialist

    **-AND-**

    5. **One** of the following:
        a) Patient is not actively participating in illicit substance abuse or alcohol abuse

        **-OR-**

        b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

        **-AND-**

    d. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 12 weeks.**

H. For the treatment of chronic hepatitis C genotype 4 infection (without decompensation) in peginterferon ineligible patients, **Sovaldi in combination with ribavirin** will be approved based on **all** of the following criteria:
    1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype infection

    **-AND-**

    2. Submission of medical records documenting evidence of chronic liver disease (at any stage of fibrosis per biopsy, radiology, or physical findings), or in the absence of chronic liver disease, serologic evidence of persistent infection for at least 6 months
    3. Patient is ineligible for treatment with peginterferon alfa, defined by at least **one** of the following:
        a) Autoimmune hepatitis or autoimmune disorders (eg, dermatomyositis, immune [idiopathic)] thrombocytopenic purpura, inflammatory bowel disease, interstitial lung disease, interstitial

nephritis, polymyositis, psoriasis, rheumatoid arthritis, sarcoidosis, and systemic lupus erythematosus)
   b) Major uncontrolled depressive illness
   c) Suicidal attempt within past year
   d) History of psychosis, schizophrenia, bipolar disorder, schizoaffective disorder, or suicidal ideation
   e) Uncontrolled seizures
   f) Moderate or severe retinopathy
   g) Poorly controlled diabetes
   h) Baseline neutrophil count below 1,500/ μL
   i) Baseline platelet count below 70,000/ μL
   j) Baseline hemoglobin below 10 g/dL
   k) Solid organ transplant (renal, heart, or lung)
   l) Significant ischemic cardiac disease
   m) Untreated thyroid disease
   n) Pregnant or unwilling to comply with adequate contraception
   o) Prior intolerance or hypersensitivity (urticaria, angioedema, bronchoconstriction, anaphylaxis, or Stevens-Johnson syndrome) to interferon therapy
   p) Symptomatic hepatitis C induced cryoglobulinemia

**-AND-**

4. Used in combination with ribavirin

**-AND-**

5. Prescribed by **one** of the following:
   a) Hepatologist
   b) Gastroenterologist
   c) Infectious Disease Specialist

**-AND-**

6. **One** of the following:
   a) Patient is not actively participating in illicit substance abuse or alcohol abuse

**-OR-**

   b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

**-AND-**

7. Patient is without decompensated liver disease (defined as Child-Pugh Class B or C)

**Authorization will be issued for 24 weeks.**

I. For the treatment of chronic hepatitis C genotype 1, 2, 3, or 4 infection in patients with hepatocellular carcinoma awaiting liver transplantation OR with decompensated liver disease, **Solvaldi in combination with ribavirin** will be approved based on **all** of the following criteria:
   1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 1, 2, 3, or 4 infection

**-AND-**

   2. Used in combination with ribavirin

**-AND-**

   3. **One** of the following:
      a) **Both** of the following:
         1) Diagnosis of hepatocellular carcinoma

**-AND-**

         2) Patient is an active candidate on the waiting list for a liver transplant

**-OR-**

b) Patient has decompensated liver disease (defined as Child-Pugh Class B or C)

**-AND-**

4. **One** of the following:
    a) Prescribed by a hepatologist, gastroenterologist, or infectious disease specialist with expertise in decompensated liver disease

    **-OR-**

    b) Patient is being managed in a liver transplant center

    **-AND-**

5. **One** of the following:
    a) Patient is not actively participating in illicit substance abuse or alcohol abuse

    **-OR-**

    b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

**Authorization will be issued for 48 weeks.**

J. For the treatment of chronic hepatitis C genotype 1 infection in patients with decompensated liver disease, **Sovaldi in combination with Olysio (simeprevir)** will be approved based on **all** of the following criteria:
    1. Submission of medical records documenting diagnosis of chronic hepatitis C genotype 1 infection

    **-AND-**

    2. Used in combination with Olysio (simeprevir)

    **-AND-**

    3. If the genotype is 1a, documentation of NS3 Q80K polymorphism testing

    **-AND-**

    4. Patient has decompensated liver disease (defined as Child-Pugh Class B or C)

    **-AND-**

    5. **One** of the following:
        a) Prescribed by a hepatologist, gastroenterologist, or infectious disease specialist with expertise in decompensated liver disease

        **-OR-**

        b) Patient is being managed in a liver transplant center

        **-AND-**

    6. **One** of the following:
        a) Patient is not actively participating in illicit substance abuse or alcohol abuse

        **-OR-**

        b) Patient is receiving substance or alcohol abuse counseling services or seeing an addiction specialist as an adjunct to HCV treatment

**Authorization will be issued for 12 weeks.**

**References:**

1. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; December 2013.
2. SVR results of a once-daily regimen of simeprevir (TMC435) plus sofosbuvir (GS-7977) with or without ribavirin in cirrhotic and non-cirrhotic HCV genotype 1 treatment-naïve and prior null responder patients: The COSMOS study. Lead Author: Ira M. Jacobson, Weill Cornell Medical College, New York, USA.
3. Olysio [package insert]. Titusville, NJ: Janssen Therapeutics; December 2013.

4. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Recommendations for Testing, Managing, and Treating Hepatitis C. January 2014. http://www.hcvguidelines.org/full-report-view. Accessed May 4, 2014.
5. Ghany MG, Strader DB, Thomas DL, Seeff LB, American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology. 2009;49(4):1335-74.
6. Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368:1867-77.
7. Jacobson IM, Ghalib RH, Rodriguez-Torres M, et al. SVR results of a once-daily regimen of simeprevir (TMC435) plus sofosbuvir (GS7977) with or without ribavirin in cirrhotic and non-cirrhotic HCV genotype 1 treatment-naive and prior null responder patients: the COSMOS study. Program and abstracts of the 64th Annual Meeting of the American Association for the Study of Liver Diseases; November 1-5, 2013; Washington, DC. Abstract LB-3.
8. Tice JA, Ollendorf DA, and Pearson SD. The Comparative Clinical Effectiveness and Value of Simeprevir and Sofosbuvir in the Treatment of Chronic Hepatitis C Infection. Published February 12, 2014 http://ctaf.org/sites/default/files/u119/CTAF_Hep_C_Apr14_final.pdf. Accessed May 4, 2014.

***Scoring Systems for Fibrosis Staging**

| **Stage (F)** | METAVIR | Batts-Ludwig | IASL** | Ishak |
|---|---|---|---|---|
| 0 | No fibrosis | No fibrosis | No fibrosis | No fibrosis |
| 1 | Periportal fibrotic expansion | Fibrosis portal expansion | Mild fibrosis | Fibrosis expansion of some portal areas with or without short fibrous septa |
| 2 | Periportal septae 1 (septum) | Rare bridges or septae | Moderate fibrosis | Fibrous expansion of most portal areas with or without short fibrous septa |
| 3 | Porto-central septae | Numerous bridges or septae | Severe fibrosis | Fibrous expansion of most portal areas with occasional portal to portal bridgingFibrous expansion of most portal areas with marked bridging (portal to portal and portal to central) |
| 4 | Cirrhosis | Cirrhosis | Cirrhosis | Fibrous expansion of most portal areas with marked bridging (portal to portal and portal to central) |
| 5 | | | | Marked bridging (portal to portal and portal to central) with occasional nodules (incomplete cirrhosis) |
| 6 | | | | Cirrhosis |

**IASL = The International Association for the Study of Liver