DRUG POLICY

Hepatitis Virus Drug Therapy

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Hepatitis Virus Drug Therapy policy is to ensure clinically suitable, cost-effective therapy for members based on product labeling, clinical guidelines and clinical studies while maintaining optimal therapeutic results. The criteria will require the use of the health plan’s preferred agents for chronic Hepatitis C therapy (Harvoni and Sovaldi) before the use of other non-preferred agents, unless there are clinical circumstances that exclude the use of Harvoni or Sovaldi, or the patient is currently receiving treatment with a non-preferred agent.

When a referral is received for a non-preferred agent, the requested agent is paid at the client’s standard specialty copay if the patient has a paid claim for the requested agent in the past 30 days. If the patient does not have a claim for the requested agent in the previous 30 days, the Post Step Therapy Criteria for Approval will be applied. If the patient meets the criteria for approval, then the requested agent is paid at the standard specialty copay.

Pegasys (peginterferon alfa 2a):

FDA-Approved Indications

- For treatment of adults with HbeAg-positive and HbeAg-negative chronic hepatitis B with compensated liver disease and evidence of viral replication and liver inflammation
- For treatment of adults with chronic hepatitis C with compensated liver disease in combination with other hepatitis C virus antiviral drugs
- Treatment of chronic hepatitis C as combination with ribavirin in patients age 5 and older with compensated liver disease
- Monotherapy for chronic hepatitis C with compensated liver disease only if the patient has contraindications/intolerances to other HCV antiviral drugs

Compendial Uses

- Acute hepatitis C infection
- Chronic myelogenous leukemia
- Giant cell tumor of the bone

PegIntron (peginterferon alfa 2b):
FDA-Approved Indications

- Monotherapy for chronic hepatitis C with compensated liver disease with contraindications/intolerances to ribavirin for adults 18 years and older that have not been previously treated (combination therapy provides substantially better response rates than monotherapy)
- In combination with ribavirin and an approved hepatitis C virus (HCV) NS3/4A protease inhibitor for adults (18 years and older) with HCV genotype 1 infection
- In combination with ribavirin in patients with HCV genotypes other than 1, pediatric patients (3 to 17 years of age), or in patients with genotype 1 infection in which use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors

Compendial uses

- Acute hepatitis C infection
- Chronic hepatitis B infection
- Chronic myelogenous leukemia

Olysio (simeprevir):

**FDA-Approved Indication**

- For adult patients with chronic HCV genotype 1 or 4 as a component of a combined antiviral treatment regimen

**Daklinza (daclatasvir)**

**FDA-Approved Indication**

- For adults with chronic HCV genotype 3 to be used in combination with sofosbuvir.

**Limitations of Use**

- Sustained virologic response rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks

**Compendial Use**

- Chronic hepatitis C genotype 1, 2 or 4 infection

Sovaldi (sofosbuvir)

**FDA-Approved Indications**

- Treatment of chronic hepatitis C for adults as a component of a combination antiviral treatment regimen for genotypes 1, 2, 3, or 4

**Compendial Uses**

- Chronic hepatitis C genotype 5 or 6 infection

**Harvoni (ledipasvir 90 mg/sofosbuvir 400 mg):** Ledipasvir is a HCV NS5A inhibitor combined with sofosbuvir, a nucleotide analog NS5B polymerase inhibitor that does not require the administration of peginterferon or ribavirin.

**FDA-Approved Indication**

- Treatment of adults with chronic hepatitis C genotype 1, 4, 5 or 6 infection
Viekira Pak (ombitasvir, paritaprevir, ritonavir fixed-dose combination tablet copackaged with dasabuvir): consists of three direct-acting antiviral medications: ombitasvir (NS5A inhibitor), paritaprevir (NS3/4A protease inhibitor), dasabuvir (non-nucleoside NS5B polymerase inhibitor) and the pharmacokinetic enhancer, ritonavir.

**FDA-Approved Indication**

- Treatment of adults with chronic hepatitis C, genotype 1 including patients with compensated cirrhosis

**Limitations of use**

- Viekira Pak is not recommended for use in patients with decompensated liver disease (Child Turcotte Pugh [CTP] Class B or C)

Technivie (ombitasvir, paritaprevir and ritonavir): consists of a fixed-dose combination of ombitasvir (NS5A inhibitor), paritaprevir (NS3/4A protease inhibitor) and the pharmacokinetic enhancer, ritonavir.

**FDA-Approved Indication**

- Treatment of adults without cirrhosis with chronic hepatitis C genotype 4 in combination with ribavirin
- May be used as monotherapy for treatment-naïve adults with chronic hepatitis C genotype 4 that have a contraindication or intolerance to ribavirin.

**Limitations of use**

- Technivie is not recommended for use in patients with moderate hepatic impairment (CTP Class B)

**POLICY**

**HEPATITIS B THERAPY**

Pegasys (peginterferon alfa-2a) and Pegintron (peginterferon alfa-2b) may be considered medically necessary for the following clinical scenarios (I-VI) when these criteria are met:

- Patient does not have decompensated liver disease (CTP Class B or C)
- Patient has not had a prior treatment failure with an HCV protease inhibitor (e.g., telaprevir, boceprevir, simeprevir, paritaprevir) despite adequate dosing and duration of therapy for patients prescribed a treatment regimen that includes an HCV protease inhibitor (eg, Olysio, Victrelis)

I. **Pegasys** (peginterferon alfa-2a) may be considered medically necessary for the treatment of adults without cirrhosis with chronic hepatitis B virus when ALL of the following criteria are met:

- HBsAg positive for at least 6 months prior to initiation of therapy
- HBeAg-negative with serum HBV-DNA > 10^4 copies/mL or > 2000 IU/mL OR HBeAg-positive with serum HBV-DNA > 10^5 copies/mL or > 20,000 IU/mL
- Persistent or intermittently elevated alanine aminotransferase (ALT) > 2x the upper limit of normal (ULN) OR liver biopsy showing chronic hepatitis with moderate to severe necroinflammation

**Approval for up to 48 weeks total**

II. **Pegasys** (peginterferon alfa-2a) may be considered medically necessary for the treatment of adults with cirrhosis with chronic hepatitis B virus when ALL of the following criteria are met:
• HBsAg positive for at least 6 months prior to initiation of therapy
• Serum HBV-DNA ≥ 10⁴ copies/mL or ≥ 2000 IU/mL

Approval for up to 48 weeks total

III. **Pegasys** (peginterferon alfa-2a) may be considered *medically necessary* for the treatment of adults with hepatitis B virus who are already receiving therapy.

Approval for up to 48 weeks total

IV. **Pegintron** (peginterferon alfa-2b) may be considered *medically necessary* for the treatment of adults without cirrhosis with chronic hepatitis B virus when ALL of the following criteria are met:
• HBsAg positive for at least 6 months prior to initiation of therapy
• HBeAg-negative with serum HBV-DNA > 10⁴ copies/mL or > 2000 IU/mL OR HBeAg-positive with serum HBV-DNA > 10⁵ copies/mL or > 20,000 IU/mL
• Persistent or intermittently elevated alanine aminotransferase (ALT) > 2x the upper limit of normal (ULN) OR liver biopsy showing chronic hepatitis with moderate to severe necroinflammation

Approval for up to 48 weeks total

V. **Pegintron** (peginterferon alfa-2b) may be considered *medically necessary* for the treatment of adults with cirrhosis with chronic hepatitis B virus when ALL of the following criteria are met:
• HBsAg positive for at least 6 months prior to initiation of therapy
• Serum HBV-DNA > 10⁴ copies/mL or > 2000 IU/mL

Approval for up to 48 weeks total

VI. **Pegintron** (peginterferon alfa-2b) may be considered *medically necessary* for the treatment of adults with hepatitis B virus who are already receiving therapy.

Approval for up to 48 weeks total

**ACUTE HEPATITIS C THERAPY**

**Pegasys** (peginterferon alfa-2a) and **Pegintron** (peginterferon alfa-2b) may be considered *medically necessary* for the following clinical scenarios (I-II) when these criteria are met:
• Patient does not have decompensated liver disease (CTP Class B or C)
• Patient has not had a prior treatment failure with an HCV protease inhibitor (e.g., telaprevir, boceprevir, simeprevir, paritaprevir) despite adequate dosing and duration of therapy for patients prescribed a treatment regimen that includes an HCV protease inhibitor (eg, Olysio, Victrelis)

I. **Pegasys** (peginterferon alfa-2a) may be considered *medically necessary* for treatment of acute Hepatitis C virus infection

Approval for up to 24 weeks total

II. **Pegintron** (peginterferon alfa-2b) may be considered *medically necessary* for:
• Treatment of acute Hepatitis C virus infection

Approval for up to 24 weeks total

**NON-HEPATITIS COMPENDIAL USES**

**Pegasys** (peginterferon alfa-2a) and **Pegintron** (peginterferon alfa-2b) may be considered *medically necessary* for the following clinical scenarios (I-II) when these criteria are met:
• Patient does not have decompensated liver disease (CTP Class B or C)
- Patient has not had a prior treatment failure with an HCV protease inhibitor (e.g., telaprevir, boceprevir, simeprevir, paritaprevir) despite adequate dosing and duration of therapy for patients prescribed a treatment regimen that includes an HCV protease inhibitor (eg, Olysio, Victrelis)

I. **Pegasys** (peginterferon alfa-2a) may be considered medically necessary for:
   - Treatment of chronic myelogenous leukemia
   - Treatment of giant cell tumor of the bone
   **Approval for up to 12 months total**

II. **PegIntron** (peginterferon alfa-2b) may be considered medically necessary for:
   - Treatment of chronic myelogenous leukemia
   **Approval for up to 12 months total**

**CHRONIC HEPATITIS C THERAPY**

The intent of this policy is to gather patient specific information to facilitate timely and appropriate therapy for patients based on product labeling, clinical studies and clinical guidelines. The criteria will require the use of the health plan’s preferred agents for chronic Hepatitis C therapy (Harvoni and Sovaldi) before the use of other non-preferred agents. If the patient has documented contraindications/intolerances or medical conditions precluding the use of Harvoni or Sovaldi, the non-preferred agent will be allowed.

**Required documentation for all Hepatitis C therapy prior authorizations:**
The provider MUST submit medical records documenting the following:
- HCV RNA pre-treatment level prior to treatment (within last 6 months)
- Treatment plan including treatment regimen and duration
- Genotype (diagnosis) and subtype (if applicable)
- Baseline or current viral load and current week of treatment
- Prior treatment regimen(s) and response(s)
- Liver transplantation status (if applicable)
- METAVIR fibrosis score (if available)
- Prior treatment regimen(s) response
- Prescriber specialty
- Q80K polymorphism testing result (if applicable)

Other appropriate information such as co-morbid disease states including but not limited to: HIV-1, Hepatitis virus B (HVB), post-organ transplant, insulin-resistant diabetes, pregnancy, renal disease, vasculitis, hemoglobinopathies and any other disease state that might increase progression of chronic HCV or influence treatment should be included in the documentation.

**PEGINTERFERON**

**Pegasys** (peginterferon alfa-2a) and **Pegintron** (peginterferon alfa-2b) may be considered medically necessary for the following clinical scenarios (I-VI) when these criteria are met:
- Patient does not have decompensated liver disease (CTP Class B or C)
- Patient has not had a prior treatment failure with an HCV protease inhibitor (e.g., telaprevir, boceprevir, simeprevir, paritaprevir) despite adequate dosing and duration of therapy for patients prescribed a treatment regimen that includes an HCV protease inhibitor (eg, Olysio, Victrelis)
- Patient has been tested and does NOT have the NS3 Q80K polymorphism when Olysio is being requested to treat chronic hepatitis virus, genotype 1a in combination with PEG-IFN and RBV

I. **PegIntron** (peginterferon alfa-2b) and **Pegasys** (peginterferon alfa-2a) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, as monotherapy or in combination with ribavirin (RBV)
II. **PegIntron** (peginterferon alfa-2b) and **Pegasys** (peginterferon alfa-2a) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection genotype 1, 3, 4, 5 or 6 in **combination with Sovaldi and RBV** for adults who are treatment-naïve or who failed prior treatment with pegylated interferon (PEG-IFN) and RBV  
**Approval for up to 48 weeks total**

III. **PegIntron** (peginterferon alfa-2b) and **Pegasys** (peginterferon alfa-2a) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection genotype 2 in **combination with Sovaldi and RBV** for adults with cirrhosis who failed prior treatment with PEG-IFN and RBV  
**Approval for up to 12 weeks total**

IV. **PegIntron** (peginterferon alfa-2b) and **Pegasys** (peginterferon alfa-2a) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection in **combination with Sovaldi and RBV** for adults with HIV coinfection who meet all the following criteria:  
- Patient meets criteria for the approval of the requested regimen  
- Patient is currently receiving antiretroviral therapy (ART) OR is ART-naïve with documented CD4 count greater than 500 cells/mm³  
- Patient will not receive treatment with tipranavir  
**Approval for up to 12 weeks total**

V. **PegIntron** (peginterferon alfa-2b) and **Pegasys** (peginterferon alfa-2a) may be considered **medically necessary** for the **initial** treatment of chronic hepatitis C virus infection, genotype 1, in **combination with Olysio and RBV** for adults without HIV coinfection who are treatment-naïve or who failed treatment with PEG-IFN and RBV AND meet one of the following criteria:  
- Genotype 1a infection without the NS3 Q80K polymorphism  
- Genotype 1b infection  
- Genotype 4 infection  
**Approval for up to 6 weeks total**

VI. **PegIntron** (peginterferon alfa-2b) and **Pegasys** (peginterferon alfa-2a) may be considered **medically necessary** for the **continuation** of therapy for the treatment of chronic hepatitis C virus infection, genotype 1 or 4, in **combination with Olysio and RBV**, when the following criteria are met:  
- Patient’s HCV-RNA < 25 IU/mL at week 4 of treatment  
**Approval for up to 14 weeks total**

- Patient’s HCV-RNA < 25 IU/mL at week 12 of treatment (Note: treatment is complete at 24 weeks for patients without a history of nonresponse to prior response to prior HCV therapy with PEG-IFN and RBV)  
**Approval for up to 24 weeks total**

- Patient’s HCV-RNA < 25 IU/mL at week 24 of treatment for patients with a history of nonresponse to prior HCV therapy with PEG-IFN and RBV  
**Approval for up to 48 weeks total**

**OLYSIO**

**Olysio** (simeprevir) may be considered **medically necessary** for the following clinical scenarios (I-XI) when these criteria are met:  
- Patient has a drug interaction/intolerance or medical condition that would preclude the use of the preferred agents, Harvoni and Sovaldi (see Appendix E)  
- Patient does not have decompensated cirrhosis/moderate or severe hepatic impairment (CTP Class B or C)

© 2016 Caremark. All rights reserved.
• Patient has not had a prior treatment failure with an HCV protease inhibitor (e.g., telaprevir, boceprevir, simeprevir, paritaprevir) despite adequate dosing and duration of therapy

I. **Olysio** (simeprevir) may be considered medically necessary for the initial treatment of chronic hepatitis C virus infection, genotype 1 or 4, in combination with PEG-IFN and RBV, for patients who are treatment-naïve or failed treatment with PEG-IFN and RBV AND meet one of the following criteria:
   - Genotype 1a infection without the NS3 Q80K polymorphism
   - Genotype 1b infection
   - Genotype 4 infection
   Approval for up to 6 weeks total

II. **Olysio** (simeprevir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1a, in combination with Sovaldi, for patients without cirrhosis who are treatment-naïve or who failed treatment with PEG-IFN and RBV
   Approval for up to 12 weeks total

III. **Olysio** (simeprevir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1a, in combination with Sovaldi, for patients with cirrhosis without the NS3 Q80K polymorphism who are treatment-naïve or failed prior treatment with PEG-IFN and RBV
   Approval for up to 24 weeks total

IV. **Olysio** (simeprevir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1b, in combination with Sovaldi, for patients without cirrhosis who are treatment naïve or failed prior treatment with PEG-INF and RBV
   Approval for up to 12 weeks total

V. **Olysio** (simeprevir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1b, in combination with Sovaldi, for patients with cirrhosis who are treatment naïve or failed prior treatment with PEG-INF and RBV
   Approval for up to 24 weeks total

VI. **Olysio** (simeprevir) may be considered medically necessary for recurrent chronic hepatitis C virus infection, genotype 1, in combination with Sovaldi +/- RBV, in patients with or without cirrhosis who are post-liver transplant
   Approval for up to 12 weeks total

VII. **Olysio** (simeprevir) may be considered medically necessary for chronic hepatitis C virus infection, in combination with Sovaldi +/- RBV, for patients with HIV coinfection that meet ALL of the following criteria:
   - Patient meets criteria for the approval of the requested regimen above
   - Patient will not receive treatment with efavirenz, etravirine, nevirapine, cobicistat or any HIV protease inhibitors
   Approval for up to 24 weeks total

VIII. **Olysio** (simeprevir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1a, in combination with Sovaldi and RBV, for patients with cirrhosis without the NS3 Q80K polymorphism who are treatment-naïve or failed prior treatment with PEG-IFN and RBV
    Approval for up to 24 weeks total
IX. **Olysio** (simeprevir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1b, in combination with Sovaldi and RBV, for patients with cirrhosis who are treatment-naïve or failed prior treatment with PEG-INF and RBV
Approval for up to 24 weeks total

X. **Olysio** (simeprevir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1, in combination with Sovaldi and RBV, for patients with cirrhosis who failed prior treatment with an HCV NS5A inhibitor and have NS5A inhibitor resistance-associated variants (RAVs) but do not have NS3A inhibitor RAVs.
Approval for up to 24 weeks total

XI. **Olysio** (simeprevir) may be considered medically necessary for the continuation of therapy for the treatment of chronic hepatitis C virus infection, genotype 1, in combination with PEG-IFN and RBV, when the following criteria is met:
- Patient’s HCV-RNA < 25 IU/mL at week 4 of treatment
Approval for up to 12 weeks total

**DAKLINZA**

Daklinza (daclatasvir) may be considered medically necessary for the following clinical scenarios (I-XX) when these criteria are met:
- Patient has a drug interaction/intolerance or medical condition that would preclude the use of the preferred agents, Harvoni and Sovaldi (see Appendix E)
- Patient is not currently taking any medications that are contraindicated such as strong inducers of CYP3A (e.g., phenytoin, carbamazepine, rifampin and St John’s wort)
- Daklinza is dosed 60 mg daily consistent with prescribing information or 90 mg daily when the patient is taking a moderate CYP3A inducers (e.g., bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin and rifapentine)

I. **Daklinza** (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 1 infection, in combination with Sovaldi, for patients without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor
Approval for up to 12 weeks total

II. **Daklinza** (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 1 infection, in combination with Sovaldi, for patients with cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor
Approval for up to 24 weeks total

III. **Daklinza** (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 2 infection, in combination with Sovaldi, for treatment naïve patients with documented anemia (baseline hemoglobin [Hgb] below 10g/dL) or RBV ineligibility (see Appendix B)
Approval for up to 12 weeks total

IV. **Daklinza** (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 2 infection, in combination with Sovaldi, for patients who failed prior treatment with sofosbuvir and ribavirin and have documented interferon ineligibility (see Appendix A)
Approval for up to 24 weeks total
V. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 3 infection, in combination with Sovaldi, for treatment naïve patients without cirrhosis
   Approval for up to 12 weeks total

VI. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 3 infection, in combination with Sovaldi, for patients with or without cirrhosis who failed prior treatment with PEG-IFN and RBV
   Approval for up to 12 weeks total

VII. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 3 infection, in combination with Sovaldi, for treatment naïve patients with cirrhosis
   Approval for up to 24 weeks total

VIII. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 3 infection, in combination with Sovaldi, for patients with or without cirrhosis who failed prior treatment with a sofosbuvir-based regimen
   Approval for up to 12 weeks total

IX. Daklinza (daclatasvir) may be considered medically necessary for the treatment of hepatitis C virus, genotype 1 or 4 infection, in combination with Sovaldi, for patients with decompensated cirrhosis (CTP class B or C) and documented anemia (baseline [Hgb] below 10 g/dL) or RBV ineligibility (see Appendix B)
   Approval for up to 24 weeks total

X. Daklinza (daclatasvir) may be considered medically necessary for the treatment of recurrent hepatitis C virus, genotype 1,3 or 4 infection, in combination with Sovaldi, for treatment naïve patients post liver transplantation and documented anemia (baseline [Hgb] below 10 g/dL) or RBV ineligibility (see Appendix B)
   Approval for up to 24 weeks total

XI. Daklinza (daclatasvir) may be considered medically necessary for the treatment of recurrent hepatitis C virus, genotype 2 infection, in combination with Sovaldi, for patients post liver transplantation and documented anemia (baseline [Hgb] below 10 g/dL) or RBV ineligibility (see Appendix B)
   Approval for up to 24 weeks total

XII. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 1 infection, in combination with Sovaldi and RBV, for treatment naïve patients with cirrhosis
    Approval for up to 24 weeks total

XIII. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 1 infection, in combination with Sovaldi and RBV, for patients with cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor
    Approval for up to 24 weeks total

XIV. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 2 infection, in combination with Sovaldi and RBV, for patients who failed prior treatment with sofosbuvir and ribavirin and have documented interferon ineligibility (see Appendix A)
    Approval for up to 24 weeks total
XV. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 3 infection, in combination with Sovaldi and RBV, for treatment naïve patients with cirrhosis
Approval for up to 24 weeks total

XVI. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 3 infection, in combination with Sovaldi and RBV, for patients with cirrhosis who failed prior treatment with PEG-IFN and RBV and have documented IFN ineligibility (see Appendix A)
Approval for up to 24 weeks total

XVII. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus, genotype 3 infection, in combination with Sovaldi and RBV, for patients who failed prior treatment with a sofosbuvir-based regimen and have documented IFN ineligibility (see Appendix A)
Approval for up to 24 weeks total

XVIII. Daklinza (daclatasvir) may be considered medically necessary for the treatment of hepatitis C virus, genotype 1, 2, 3 or 4 infection, in combination with Sovaldi and RBV, for patients with decompensated cirrhosis (CTP class B or C)
Approval for up to 12 weeks total

XIX. Daklinza (daclatasvir) may be considered medically necessary for the treatment of recurrent hepatitis C virus infection, in combination with Sovaldi and RBV, for patients who are post liver transplantation
Approval for up to 12 weeks total

XX. Daklinza (daclatasvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, in combination with Sovaldi +/- RBV, for patients with HIV coinfection who meet the criteria for approval for the requested regimen above.
Approval for up to 24 weeks total

SOVALDI

Sovaldi (sofosbuvir) may be considered medically necessary for the following clinical scenarios (I-XVI) when the patient has not had a prior treatment failure with an HCV protease inhibitor (e.g., telaprevir, simeprevir, boceprevir and paritaprevir) despite adequate dosing and duration of therapy for patients requesting treatment regimen with Olysio.

I. Sovaldi (sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1, 3, 4, 5 and 6, in combination with PEG-IFN and RBV, for patients who are treatment-naïve or who have failed prior treatment with PEG-IFN and RBV
Approval for up to 12 weeks total

II. Sovaldi (sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 2, in combination with PEG-IFN and RBV, for patients who failed prior treatment with PEG-IFN and RBV or with sofosbuvir and RBV
Approval for up to 12 weeks total

III. Sovaldi (sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 3, in combination with PEG-IFN and RBV, for patients who failed prior treatment with sofosbuvir and RBV
Approval for up to 12 weeks total

© 2016 Caremark. All rights reserved.
IV. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotype 1, *in combination with RBV*, for patients who have a documented interferon (IFN) ineligibility (see Appendix A)  
*Approval for up to 24 weeks total*

V. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotype 2, *in combination with RBV*, for patients without cirrhosis who are treatment-naïve  
*Approval for up to 12 weeks total*

VI. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotype 2, *in combination with RBV*, for patients with cirrhosis who are treatment-naïve  
*Approval for up to 16 weeks total*

VII. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotype 2, *in combination with RBV*, for patients without cirrhosis who failed prior treatment with PEG-IFN and RBV  
*Approval for up to 16 weeks total*

VIII. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotype 2, *in combination with RBV*, for patients with cirrhosis who failed prior treatment with PEG-IFN and RBV  
*Approval for up to 24 weeks total*

IX. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotype 3, *in combination with RBV*, for patients with documented IFN ineligibility (see Appendix A) who are treatment-naïve  
*Approval for up to 24 weeks total*

X. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotype 4, *in combination with RBV*, for patients who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV  
*Approval for up to 24 weeks total*

XI. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of chronic hepatitis C virus infection, genotypes 1, 2, 3 or 4, *in combination with RBV*, for patients with hepatocellular carcinoma awaiting liver transplantation who meet MILAN criteria, defined as the following:  
- Tumor size 5 centimeters or less in diameter with single hepatocellular carcinomas OR 3 tumor nodules or less, each 3 cm or less in diameter with multiple tumors AND  
- No extrahepatic manifestations of the cancer or evidence of vascular invasion of tumor  
*Approval up to 48 weeks total or until liver transplantation (whichever is first)*

XII. **Sovaldi** (sofosbuvir) may be considered *medically necessary* for the treatment of recurrent chronic hepatitis C virus infection, genotypes 2 or 3, *in combination with RBV*, for patients who are post liver transplant  
*Approval up to 24 weeks total*
XIII. **Sovaldi** (sofosbuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 2 or 3, **in combination with RBV**, for patients with decompensated cirrhosis (CTP Class B or C)

**Approval up to 48 weeks total**

XIV. **Sovaldi** (sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, **in combination with Olysio +/- RBV**, for patients prescribed Sovaldi in combination with Olysio (with or without RBV as applicable) who meet the criteria for approval for the requested regimen. Refer to the Olysio criteria above for the specific criteria for approval and approval durations.

XV. **Sovaldi** (sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, **in combination with Daklinza +/- RBV**, for patients prescribed Sovaldi in combination with Daklinza (with or without RBV as applicable) who meet the criteria for approval for the requested regimen. Refer to the Daklinza criteria above for the specific criteria for approval and approval durations.

XVI. **Sovaldi** (sofosbuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection in patients with HIV coinfection that meet ALL of the following criteria:

- Patient meets criteria for the approval of the requested regimen above
- Patient will not receive treatment tipranavir

**HARVONI**

**Harvoni** (ledipasvir and sofosbuvir) may be considered **medically necessary** for the following clinical scenarios (I-XIV) when the patient will not be taking any other drugs containing sofosbuvir (Sovaldi).

I. **Harvoni** (ledipasvir and sofosbuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 1, for patients with or without cirrhosis who are treatment-naive

**Approval for up to 12 weeks total**

*Treatment for 8 weeks can be considered in treatment-naive patients without cirrhosis who have pre-treatment HCV RNA below 6 million IU/mL*

II. **Harvoni** (ledipasvir and sofosbuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 1, for patients without cirrhosis who have failed prior treatment with PEG-IFN and RBV with or without a HCV protease inhibitor

**Approval for up to 12 weeks total**

III. **Harvoni** (ledipasvir and sofosbuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 1, for patients with cirrhosis who are have failed prior treatment with PEG-IFN and RBV with or without a HCV protease inhibitor

**Approval for up to 24 weeks total**

IV. **Harvoni** (ledipasvir and sofosbuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 4, 5 or 6, for patients who are treatment-naive or have failed prior treatment with PEG-IFN and RBV with or without a HCV protease inhibitor

**Approval for up to 12 weeks total**

V. **Harvoni** (ledipasvir and sofosbuvir) may be considered **medically necessary** for the treatment of recurrent chronic hepatitis C virus infection, genotype 1 or 4, for treatment-naive patients who are post
liver transplant with documented anemia (baseline HBG below 10g/dL) or RBV ineligibility (see Appendix B)

Approval for up to 24 weeks total

VI. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1, in combination with RBV, for patients with cirrhosis who have failed prior treatment with PEG-IFN and RBV with or without a HCV protease inhibitor

Approval for up to 12 weeks total

VII. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1, in combination with RBV, for patients without cirrhosis who have failed prior treatment with a sofosbuvir-containing regimen (e.g., sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV or sofosbuvir plus simprevir with or without RBV)

Approval for up to 12 weeks total

VIII. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1, in combination with RBV, for patients with cirrhosis who have failed prior treatment with a sofosbuvir-containing regimen (e.g., sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV or sofosbuvir plus simprevir with or without RBV)

Approval for up to 24 weeks total

IX. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1, in combination with RBV, for patients with cirrhosis who have failed prior treatment with an HCV NS5A inhibitor and do not have any NS5A resistance-associated variants (RAVs)

Approval for up to 24 weeks total

X. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1 or 4, in combination with RBV, for patients with decompensated cirrhosis (CTP class B or C)

Approval for up to 12 weeks total

XI. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 1 or 4, in combination with RBV, for patients with decompensated cirrhosis (CTP class B or C) who have failed prior treatment with a sofosbuvir-containing regimen (e.g., sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV or sofosbuvir plus simprevir with or without RBV)

Approval for up to 24 weeks total

XII. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of recurrent chronic hepatitis C virus infection, genotype 1 or 4, in combination with RBV, for patients with decompensated cirrhosis (CTP class B or C) who are post liver transplant

Approval for up to 12 weeks total

XIII. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of recurrent chronic hepatitis C virus infection, genotype 1 or 4, in combination with RBV, for patients who are post liver transplant

Approval for up to 12 weeks total

XIV. Harvoni (ledipasvir and sofosbuvir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection for patients with HIV coinfection that meet ALL the following criteria:
• Patient meets criteria for the approval of the requested regimen above
• Patient will not receive treatment tipranavir
• Patient will not receive treatment with cobicistat given with tenofovir disoproxil fumarate

**VIEKIRA PAK**

**Viekira Pak** (ombitasvir/paritaprevir/ritonavir with dasabuvir) may be considered **medically necessary** for the following clinical scenarios (I-VI) when these criteria are met:

- Patient has a drug interaction/intolerance or medical condition that would preclude the use of the preferred agents, Harvoni and Sovaldi (see Appendix E)
- Patient has not had a prior treatment failure with an HCV protease inhibitor (e.g., telaprevir, simeprevir, boceprevir and paritaprevir) despite adequate dosing and duration of therapy
- Patient does not have decompensated liver disease (CTP Class B or C)
- Patient is not currently taking any medications that are highly dependent on CYP3A for clearance, strong inducers of CYP3A and CYP2C8, or strong inhibitors of CYP2C8 (see Appendix C)

I. **Viekira Pak** may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 1a (or unknown subtype), **in combination with RBV**, for patients without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV
   **Approval for up to 12 weeks total**

II. **Viekira Pak** may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 1a (or unknown subtype), **in combination with RBV**, for patients with cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV
    **Approval for up to 24 weeks total**

III. **Viekira Pak** may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 1b, **in combination with RBV**, for patients with cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV
    **Approval for up to 12 weeks total**

IV. **Viekira Pak** may be considered **medically necessary** for the treatment of recurrent chronic hepatitis C virus infection, genotype 1 (irrespective of subtype), **in combination with RBV**, for patients who are post liver transplant with a Metavir fibrosis score of 2 or lower
   **Approval for up to 24 weeks total**

V. **Viekira Pak** (ombitasvir/paritaprevir/ritonavir with dasabuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection, genotype 1b, without RBV, for patients with or without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV
   **Approval for up to 12 weeks total**

VI. **Viekira Pak** (ombitasvir/paritaprevir/ritonavir with dasabuvir) may be considered **medically necessary** for the treatment of chronic hepatitis C virus infection for patients with HIV coinfection that meet ALL the following criteria:
- Patient meets criteria for the approval of the requested regimen above
- Patient is currently receiving antiretroviral therapy
- Patient will not receive treatment with efavirenz, rilpivirine, darunavir or ritonavir-boosted lopinavir, atazanavir or ritonavir-boosted atazanavir

**TECHNIVIE**
Technivie (ombitasvir, paritaprevir and ritonavir) may be considered medically necessary for the following clinical scenarios (I-III) when these criteria are met:

- Patient has a drug interaction/intolerance or medical condition that would preclude the use of the preferred agents, Harvoni and Sovaldi (see Appendix E)
- Patient has not tried and failed an HCV protease inhibitor (e.g., telaprevir, boceprevir, simeprevir, paritaprevir despite adequate dosing and duration of therapy
- Patient is not currently taking any medications that are highly dependent on CYP3A for clearance or are moderate or strong inducers of CYP3A (see Appendix D)
- Patient does not have moderate or severe hepatic impairment (Child-Pugh B or C)

I. Technivie (ombitasvir, paritaprevir and ritonavir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 4, in combination with RBV, for patients without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV

Approval for up to 12 weeks total

II. Technivie (ombitasvir, paritaprevir and ritonavir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection, genotype 4, without RBV, for patients without cirrhosis who are treatment-naïve and are intolerant to RBV with documented anemia (baseline hemoglobin below 10g/dL) or RBV ineligibility (see Appendix B)

Approval for up to 12 weeks total

III. Technivie (ombitasvir, paritaprevir and ritonavir) may be considered medically necessary for the treatment of chronic hepatitis C virus infection for patients with HIV coinfection that meet ALL the following criteria:
- Patient meets criteria for the approval of the requested regimen above
- Patient is currently receiving antiretroviral therapy
- Patient will not receive treatment with efavirenz, rilpivirine, darunavir or ritonavir-boosted lopinavir, atazanavir, or ritonavir-boosted atazanavir.

ALL of the aforementioned drugs are considered not medically necessary for patients who do not meet the criteria set forth above.

APPENDIX A: INTERFERON INELIGIBILITY
Interferon ineligibility is defined as one or more of the below:
- Intolerance to interferon
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to PEG-IFN or any of its components
- Major uncontrolled depressive illness
- A baseline platelet count < 90,000/mcL
- A baseline hemoglobin < 10g/dL
- History of pre-existing cardiac disease

APPENDIX B: RIBAVIRIN INELIGIBILITY
Ribavirin ineligibility is defined as one or more of the below:
- Pregnant female or male who’s female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine

APPENDIX C: DRUGS CONTRAINDICATED WITH VIEKIRA PAK:
- Alfuzosin
• colchicine
• carbamazepine
• phenytoin
• phenobarbital
• gemfibrozil
• rifampin
• ergot derivatives (ergotamine, dihydroergotamine, ergonovine, methylergonovine)
• ethinyl estradiol-containing medications (e.g., Lo Loesterin Fe, Ortho Tri-Cyclen Lo, Ortho Evra, Nuva Ring)
• St. John’s wort
• lovastin
• simvastatin
• pimozide
• efavirenz
• sildenafil or Revatio when used for the treatment of Pulmonary Hypertension (PAH)
• triazolam
• midazolam (oral administration)

APPENDIX D: DRUGS CONTRAINDICATED WITH TECHNIVIE:
• Alfuzosin
• colchicine
• carbamazepine
• phenytoin
• phenobarbital
• rifampin
• ergot derivatives (ergotamine, dihydroergotamine, ergonovine, methylergonovine)
• ethinyl estradiol-containing medications (e.g., Lo Loesterin Fe, Ortho Tri-Cyclen Lo, Ortho Evra, Nuva Ring)
• St. John’s wort
• lovastin
• simvastatin
• pimozide
• efavirenz
• sildenafil or Revatio when used for the treatment of Pulmonary Hypertension (PAH)
• triazolam
• midazolam (oral administration)

APPENDIX E:
When a referral is received for a non-preferred agent, the requested agent is paid at the client’s standard specialty copay if the patient has a paid claim for the requested agent in the past 30 days. If the patient does not have a claim for the requested agent in the previous 30 days, the Post Step Therapy Criteria for Approval will be applied. If the patient meets the criteria for approval, then the requested agent is paid at the standard specialty copay.

Prior approval is required. Submit a prior approval/treatment request now.
Quantity limits apply:

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Generic Name</th>
<th>Quantity Limit</th>
</tr>
</thead>
</table>

© 2016 Caremark. All rights reserved.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Type: Peginterferon alpha-2b/alpha-2a</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>PegIntron®</td>
<td></td>
<td>Redipen® or vial: 4 per 28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Redipen® Pak: 1 per 28 days</td>
</tr>
<tr>
<td>Pegasys®</td>
<td></td>
<td>Proclick™ autoinjector or vial: 4 per 28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proclick™ autoinjector or prefilled syringe Monthly Convenience Pack: 1 per 28 days</td>
</tr>
<tr>
<td>Harvoni®</td>
<td>ledipasvir-sofosbuvir</td>
<td>28 tablets per 28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lifetime maximum of 168 tablets</td>
</tr>
<tr>
<td>Olysio™</td>
<td>simeprevir</td>
<td>28 capsules per 28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lifetime maximum of 168 capsules</td>
</tr>
<tr>
<td>Sovaldi™</td>
<td>sofosbuvir</td>
<td>28 tablets per 28 days</td>
</tr>
<tr>
<td>Viekira Pak™</td>
<td>ombitasvir-paritaprevir-ritonavir-dasabuvir</td>
<td>120 tablets per 28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lifetime maximum of 672 tablets</td>
</tr>
<tr>
<td>Daklinza™</td>
<td>daclatasvir</td>
<td>28 tablets per 28 days</td>
</tr>
<tr>
<td>Technivie™</td>
<td>Ombitasvir - Paritaprevir - Ritonavir</td>
<td>28 tablets per 28 days</td>
</tr>
</tbody>
</table>

**CLINICAL RATIONALE**

Patients with chronic HCV are treated clinically based on the genotype. Genotype 1 represents approximately 70% of HCV illness in the United States, followed by genotype 2 at 15 to 20%, genotype 3 at 10 to 12%, genotype 4 at 1% and genotype 5 and 6 with less than 1%. Among genotype 1 infections, genotype 1a is estimated to account for 55% of infections.

**Peginterferon and Ribavirin**

Interferon alfa has been the mainstay of treatment for chronic hepatitis C since its introduction in the mid-1980s. In 2001, the first pegylated interferon was approved and allowed for a once a week dosing. This pegylated form of interferon combined with ribavirin, increased sustained viral response (SVR) to greater than 50% versus the 35 to 40% previously seen with interferon alfa. Peginterferon and ribavirin are often components of other therapies used to increase efficacy. Use of any medications with ribavirin may cause birth defects and fetal death. Monthly pregnancy tests and two forms of contraception should be used to avoid pregnancy while using ribavirin during treatment (male and female patients).
Non-hepatitis related uses of Peginterferon alfa: The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium™ is also under frequent updates. Currently peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (Peglntron) is recommended for Chronic Myelogenous Leukemia (CML) at a recommendation of 2A.

Per the National Cancer Institute, treatment for Chronic Myeloproliferative Neoplasm (CMN) conditions such as polycythemia vera, essential thrombocythemia, primary myelofibrosis, chronic neutrophil leukemia, chronic eosinophilic leukemia, interferon-alfa and peginterferon-alfa have been used. Peginterferon alfa-2a (Pegasys) also has supporting evidence for use in patients with myeloproliferative disorders (MPD). In a phase II study of 79 patients, the overall hematologic response rate was 80% in PV and 91% in ET for patients using peginterferon alfa-2a. This study demonstrated that peginterferon alfa-2a resulted in remarkable clinical activity, high rates of molecular response and acceptable toxicity in patients with advanced ET or PV.

NS3/4A protease inhibitors (first-generation)
In 2011, when Incivek (telaprevir) and Victrelis (boceprevir) were FDA approved and entered the market, the standard of care for HCV genotype 1 became a triple therapy regimen containing peginterferon alfa, ribavirin and a protease inhibitor (either Incivek or Victrelis). The introduction of these first-generation protease inhibitors offered SVR rates of 50 to 70% but still required long treatment durations of 24 to 48 weeks and had several adverse effects. Incivek ceased production and is not longer for sale in the United States as of October 16, 2014. Currently, Victrelis is no longer a recommended treatment for CHC, genotype 1 due to lower SVR rates and high rates of adverse events compared to the currently available therapies. In January of 2015, Merck Sharpe and Dohme announced discontinuation of Victrelis and estimated product availability will be until December of 2015.

NS3/4A protease inhibitor (second-generation)
Olysio (simpervir), a once-a-day second-generation protease inhibitor, was approved in November of 2013 by the FDA for the treatment of CHC genotype 1 to be used as a part of a triple therapy regimen with peginterferon alfa and ribavirin. Patients with genotype 1, subtype a, need to be tested for Q80K polymorphism prior to initiation of treatment as these patients have a substantially reduced rate of response to treatment. It is strongly recommended that alternative therapies be considered in patients with Q80K polymorphism present. Efficacy of Olysio has not been established for patients that have previously failed with a treatment regimen that includes other HCV NS3/4A protease inhibitors. Key trials that were used for FDA approval were QUEST-1 and QUEST-2 in the treatment-naïve population and PROMISE in the treatment-experienced population. QUEST-1 and QUEST-2 showed overall SVR12 (sustained virologic rate at 12 weeks after therapy is complete) of 80% in patients treated with Olysio for 12 weeks plus peginterferon and ribavirin (peginterferon and ribavirin continued for 12 to up to 48 weeks depending upon response guided therapy) versus placebo plus peginterferon and ribavirin for 48 weeks that demonstrated 50-51% SVR12. The PROMISE trial demonstrated a 79% SVR12 in treatment-experienced patients that had previously relapsed from peginterferon and ribavirin therapy versus 37% SVR12 in the placebo arm. Adverse events of skin reactions (itching), anemia and elevated bilirubin were higher in Olysio arms versus placebo. Olysio has not been studied in patients with an estimated creatinine clearance of less than 30 ml/min., patients with end stage renal disease including those requiring dialysis. Olysio is not recommended for use with ribavirin and peginterferon in patients that have decompensated cirrhosis (moderate or severe hepatic impairment). Use of Olysio is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh Class B or C).

On November 5, 2014, Olysio was FDA approved to be used in combination with sofosbuvir for patients without cirrhosis that are treatment-naïve or treatment-experienced with previous interferon-based regimens for 12 weeks. It also received approval for the patients with cirrhosis that are treatment-naïve and treatment experienced for 24 weeks. This approval was based on the COSMOS study. Overall, in a group of 167 patients with Hepatitis C, genotype 1, the SVR12 was 93% in patients being treated with the
combination of simeprevir 150mg daily/sofosbuvir 400mg daily with or without ribavirin for 12 weeks. These patients were divided into two cohorts. The first cohort included 80 patients that had failed to achieve a cure with prior therapy (pegylated-interferon and ribavirin) and had moderate or no fibrosis of the liver. Reported SVR12 was 93% without ribavirin and 96% with ribavirin. The second cohort included 87 patients that were either treatment-naïve or failed to achieve a cure with prior therapy (pegylated interferon and ribavirin) and patients with advanced fibrosis or compensated cirrhosis (SVR12=93%). When the treatment arms with and without ribavirin are combined, the overall SVR12 rate was 95% (61/64) (Metavir F0-F3) in the 12 week treatment arm and 96% (22/23) with Metavir F4 for the 24 week treatment arm. Ribavirin was not found to increase response.

Per prescribing information, no dosage adjustment of Olysio is required for patient with mild, moderate or renal impairment. The safety and efficacy of Olysio has not been studied in chronic hepatitis C infected patients with severe renal impairment or end-stage renal disease, including patients requiring dialysis. Olysio is not recommended for patient with moderate or severe hepatic impairment (Child-Pugh Class B or C). Olysio in combination with peg-interferon and ribavirin is contraindicated in patients with decompensated cirrhosis (Child-Pugh Class B or C).

**NS5A inhibitor**

Daklinza (daclatasvir) is a NS5A inhibitor approved by the FDA for patients 18 years of age and older to use in combination with sofosbuvir for the treatment of CHC genotype 3 as part of a dual therapy regimen. Daklinza was approved based on the phase 3 ALLY-3 clinical open-labeled trial. This trial included 152 subjects that were treatment-naïve (n=101) and treatment experienced (n=51). The majority of treatment-experienced patients were failures on prior treatment of peginterferon/ribavirin, although 7 patients had failed a previous sofosbuvir regimen and 2 failed an investigational cyclophilin regimen. Previous treatment-experience failures with a NS5A inhibitor agents were not allowed in the study. Subjects received Daklinza 60mg daily and sofosbuvir 400mg daily for 12 weeks and were followed for 24 weeks post treatment. Treated subjects had a median age of 55 years, 59% were male, 90% white and 21% had compensated cirrhosis. Overall successful SVR treatment outcome, was 89% (135/152), with 96% (115/120) for noncirrhotic subjects and 63% (20/32) for subjects with cirrhosis. In a breakdown of treatment-naïve versus treatment-experienced subjects, the treatment-naïve group reported an SVR of 90% (91/101) and treatment-experienced group an SVR of 86% (44/51). Treatment-naïve subject with cirrhosis reported an SVR of 58% (11/19) versus 98% (80/82) for noncirrhotic patients. Treatment-experienced subjects also reported lower SVRs in the cirrhotic group of 69% (9/13) versus 92% (35/38) for noncirrhotic patients. Limitations of use as listed per the prescribing information: Sustained virological response (SVR) rates are reduced in patients with cirrhosis. One patient reported an on-treatment virological failure in the treatment-naïve group (1%).

Dosage and administration for Daklinza is 60 mg by mouth daily with or without food in combination with sofosbuvir 400mg by mouth daily for 12 weeks. For patients taking strong CYP3A inhibitors, dosage should be reduced to 30 mg daily and for patients taking moderate CYP3A inducers, dosage is 90 mg daily. Use with strong CYP3A inducers is contraindicated. Patients taking drugs that are moderate CYP3A inhibitors can have increased concentrations of daclatasvir and should be monitored closely for potential adverse events.

No dosage adjustments are necessary for patients with renal impairment or mild, moderate or severe liver impairment. Safety and efficacy have not been established in patients with decompensated cirrhosis or the use of Daklinza combination therapy in liver transplant patients.

**NS5B polymerase inhibitor**

Sovaldi is an NS5B polymerase inhibitor approved by the FDA in December of 2013 for the treatment CHC genotypes 1 and 4 as part of a triple therapy regimen with peginterferon alfa and ribavirin, and for genotypes
2 and 3 as part of a dual therapy regimen with ribavirin. If peginterferon alfa is contraindicated for genotype 1, Sovaldi can be used with ribavirin as part of a dual therapy regimen with a longer duration. Sovaldi’s approval also included patients who had hepatocellular carcinoma (HCC) meeting Milan criteria (awaiting liver transplantation) and for those who are co-infected with HIV-1. The standard of care for genotype 1 was changed with the approval of Sovaldi and Olysio by improving cure rates to 80 to 90% and providing shorter courses of therapy. Sovaldi was approved based on several trials. Efficacy for genotype 1 was demonstrated in the NEUTRINO and PHOTON-1 trials with SVR of 89% (combined with ribavirin and peginterferon in a treatment-naïve population) for 12 weeks and 76% (with ribavirin) for 24 weeks (treatment-naïve and HIV-1 co-infected). Studies including treatment for genotype 2 and 3, included FISSION, POSITRON, FUSION, VALENCE and PHOTON-1. Efficacy for genotype 2 with ribavirin, ranged from 86% to 97% including treatment-naïve, interferon ineligible and treatment-experienced failures on past regimens of interferon and ribavirin. Genotype 3, treated with daily sofosbuvir with ribavirin showed the best efficacy for treatment at 24 weeks with SVR of 84%. Treatment-naïve patients with cirrhosis demonstrated a SVR of 92% and treatment-experienced demonstrated an SVR of 62% (VALENCE). Trials for genotype 3 that had treatment durations with sofosbuvir and ribavirin of 12 weeks, had a decreased efficacy and were not approved by the FDA. Patients with genotype 4 were trialed with the addition of interferon and ribavirin for 12 weeks and reported SVR of 96%. Genotype 5 and 6 were also tested in the NEUTRINO trial and although there was promising data of 100% SVR, due to the low numbers of patients, genotype 5 (one patient) and genotype 6 (6 patients), treatment was not FDA approved. Adverse events were significantly less in the Sovaldi treatment groups that did not use peginterferon and similar to placebo except in regard to fatigue (placebo 24%, Sovaldi and ribavirin for 12 weeks 38% and Sovaldi and ribavirin for 24 weeks at 30%).

In March of 2105, the FDA issued a warning that serious bradycardia can occur when amiodarone is taken with Sovaldi or when taken in combination with another direct acting antiviral such as daclatasvir or simeprevir (Olysio). It is the current recommendation that these drugs should not be prescribed together.

Per the prescribing information, no dosing recommendation can be made for patients with end-stage renal disease or severe renal impairment (estimated creatinine clearance less than 30 mL/min/1.73m²). No dosage adjustment is necessary for patients with Child-Pugh A, B or C. Safety and efficacy have not been established for patients with decompensated cirrhosis.

**Fixed-dose combination therapies**

**Harvoni (NS5A inhibitor-ledipasvir and NS5B polymerase inhibitor-sofosbuvir)**

Harvoni is the first all-oral, interferon and ribavirin-free treatment regimen to receive FDA approval in October of 2014. It is a single pill, fixed-dose combination of ledipasvir 90mg (NS5A inhibitor) combined with sofosbuvir 400mg (NS5B polymerase inhibitor). It is currently FDA approved for genotype 1 patients only. It offers an opportunity for a shorter treatment course of 8 weeks for treatment-naïve patients with a HCV RNA level of less than 6 million UI/mL. It also was tested in patients that had failed previous therapies of pegylater interferon plus ribavirin with or without a protease inhibitors (telaprevir, boceprevir and simeprevir). Harvoni was approved based of the ION studies. The overall SVR reported in ION-1 (treatment-naïve patients with and without cirrhosis) was 99% (treatment duration of 12 weeks), overall SVR reported in ION-2 (treatment experienced with PEG/IFN or PEG/IFN/PI with or without cirrhosis) for the patients without cirrhosis was 94% and with cirrhosis 99% (12 and 24 week duration respectively) and an overall SVR for ION-3 (treatment-naïve without cirrhosis) for 8 weeks (HCV RNA less than 6 million UI/ml) was 94% and for 12 weeks was 96%. Adverse events were minimal with fatigue, headache and nausea being the most commonly reported. The ION trials did not include patients experienced with co-infections of
hepatitis B or HIV-1, genotypes other than 1, alcohol/drug abuse, decompensated cirrhosis and post-liver transplantation.

The ERADICATE trial is a Phase 2b open-label study in chronic HCV patients that are treatment-naive, with HIV co-infection without cirrhosis treated with Harvoni for 12 weeks. Patients were in two cohorts of antiretroviral (ARV) treated (n=13) and ARV untreated (n=37). ARVs used in the trial were tenofovir-emtricitabine, efavirenz, raltegravir, rilpivirine, rilpivirine-raltegravir and efavirenz–raltegravir. The ARV treatment group was followed through the 12 weeks of treatment and had suppression of the HCV-RNA level, 98% of patients (49/50) achieved SVR12 (both cohorts), with the one patient showing an early relapse at SVR2.

ELECTRON 2 is a phase 2 open-label study that divided Harvoni treatments into three cohorts: Genotype 1 (treatment-naïve and experienced) that relapsed with prior sofosbuvir therapy (Cohort 1); patients with Child-Pugh Class B hepatic impairment (Cohort 2) and genotype 3 (treatment-naïve patients) (Cohort 3) treated for 12 weeks. Preliminary results of the trial: Cohort 1 used add-on of RBV and achieved 100% SVR12 (19/19 patients), Cohort 2 achieved 65% SVR12 (13/20) and Cohort 3 (genotype 3) was subdivided into add-on RBV to Harvoni and Harvoni alone. The Harvoni group without RBV achieved 64% SVR12 (16/25) and the Harvoni plus RBV achieved 100% SVR12 (26/26).

SOLAR-1 was a large multicenter randomized controlled trial of 223 liver transplant patients with Hepatitis C with genotypes 1 and 4 in various stages of fibrosis. Harvoni was dosed with ribavirin for 12 and 24 weeks. SVR was achieved in 96% of patients (Metavir stage F0-F3) and 96% in those with compensated cirrhosis in both treatment arms. Since all patient received ribavirin it is presumed that it is contributory to the high SVR rate. SOLAR-2 was a multicenter randomized controlled trial of 108 patients with Hepatitis C with genotypes 1 and 4 with decompensated cirrhosis. Excluding 6 patients who had received a transplant, SVR was achieved in 87% of the 12 week treatment course with ribavirin and 89% in the 24 week treatment course.

In March of 2105, the FDA issued a warning that serious bradycardia can occur when amiodarone is taken with either Harvoni or when taken in combination with another direct acting antiviral such as daclatasvir or simeprevir (Olysio). It is the current recommendation that these drugs should not be prescribed together.

Per the prescribing information, no dosing recommendation can be made for patients with end-stage renal disease requiring hemodialysis or severe renal impairment (estimated creatinine clearance less than 30 mL/min/1.73m²). No dosage adjustment is necessary for patients with Child-Pugh A, B or C. safety and efficacy of Harvoni has not been established in patients with decompensated cirrhosis.

**Viekira Pak**

(NS5A inhibitor-ombitasvir, NS3/4A protease inhibitor-paritaprevir, nonnucleoside NS5B polymerase inhibitor-dasabuvir plus a CYP3A inhibitor/pharmacokinetic enhancer-ritonavir)

Viekira Pak is an FDA approved treatment for genotype 1 patients available without the use of interferon. It is approved for treatment-naïve, treatment-experienced patients with or without cirrhosis and post-liver transplant patients with normal hepatic function with mild fibrosis (Metavir fibrosis score 2 or less). Ribavirin is part of dual therapy for all patients except genotype 1b without cirrhosis. Duration of therapy ranges from 12 weeks to 24 weeks depending upon genotype with or without cirrhosis and/or liver transplant. Eight major phase 3 trials were used for FDA approval, SAPPHIRE-I, TURQUOISE-II, PEARL-III and PEARL-IV in treatment-naïve and SAPPHIRE-II, TURQUOISE-II and PEARL-II in treatment experienced patients. Treatment-experienced patients were defined as patient that had failed on a previous regimen of peginterferon and ribavirin. The TURQUOISE-II trial population included patients with and without cirrhosis, TURQUOISE-I included HIV-1 co-infected subjects and the CORAL-I trial was based on liver transplant
patients. Overall SVR results ranged from 90 to 100%. In TURQUOISE-II, 12 week arm, patients with genotype 1a achieved and SVR12 of 89% while patients in the 24 week arm achieved an SVR of 94%. SAPPHIRE-I and II, PEARL-II, III and IV and TURQUOISE II studies did not include patients that were Hepatitis B coinfected.

TURQUOISE-I, a study with 63 patients that were co-infected with HCV-1, genotype 1 and human immunodeficiency virus (HIV-1) and were stable on HIV-1 antiretroviral therapy, were treated with Viekira Pak and ribavirin for 12 and 24 weeks. Reported SVR12 rates were 93.5% (29/31) in the 12 week arm and 90.6% (29/32) in the 24 week arm. In a breakdown by subtype, the SVR12 rate for 1a patients was 91% (51/56) and 1b was 100% (7/7).

CORAL-I was a study with post-liver transplant patients without cirrhosis with normal hepatic function that were treated with Viekira Pak within one year of transplant and achieved SVR12 and sustained virologic response 24 weeks post treatment (SVR24) of 97.1% (33 of 34 patients). In a breakdown by subtype, the SVR rate for 1a patients was 97% (28/29) and 1b was 100% (5/5).

No dosage adjustment is necessary for patients with mild to severe renal function impairment with Viekira Pak although it has not been studied in patients on dialysis. Viekira Pak does not require dose adjustment for patient with mild hepatic impairment (Child-Pugh A), it is not recommended for patients with moderate hepatic impairment (Child-Pugh B) and is contraindicated for use in patients with severe hepatic impairment (Child-Pugh C).

Technivie (NS5A inhibitor-ombitasvir, NS3/4A protease inhibitor-paritaprevir and a CYP3A inhibitor/pharmacokinetic enhancer-ritonavir)

Technivie was FDA approved for treatment of CHC patients with genotype 4. Safety and efficacy is based on the PEARL-I, a randomized open-labeled trial of 135 patients that were treatment-naïve or treatment-experienced with peginterferon/ribavirin without cirrhosis. Previous exposure to hepatitis C direct acting antivirals was prohibited. The median age was 51 years, 64% were treatment-naïve, 17% were prior peginterferon/ribavirin null responders, 7% were prior peginterferon/ribavirin partial responders, 13% were prior peginterferon/ribavirin relapsers and 65% were male.

Overall SVR12 study results for treatment-naïve (n=42) and treatment experienced patients (n=49) that received Technivie with ribavirin was 100%. Treatment-naïve patients that received Technivie alone for 12 weeks reported an SVR12 of 91% (40/44). Of the four patients that did not achieve SVR12, one was an on-treatment failure, two had relapsed before or during the 12 week time period and one was lost in follow-up. Technivie without ribavirin may be considered for treatment-naïve patients without cirrhosis. Ribavirin is contraindicated for patients with hemoglobinopathies, coadministration with didanosine or during pregnancy, including males with female partners that are pregnant. Patients that have had hypersensitivity reactions to ribavirin such as Stevens-Johnson syndrome, topic epidermal necrolysis and erythema multiforme should avoid use.

The 131 subjects that achieved SVR12 were followed throughout post-treatment week 24. Data was available on 129 subjects and 100% of these maintained SVR at 24 weeks.

Treatment options in patients with decompensated cirrhosis, pre- and post-transplant remaining challenging. In patients with decompensated cirrhosis who are not candidates for liver transplant, the only chance to improve or stabilize liver function is to eradicate the HCV with an interferon-free regimen. This eradication may provide clinical improvement and increased survival.

Patients awaiting liver transplant with advanced cirrhosis are considered one of the most difficult-to-treatment populations. Although the best treatment regimen has not been defined, a combination of
sofosbuvir with a second direct acting agent (DAA) such as ledipasvir, simeprevir or daclatasvir will be an option depending upon genotype. Interferon-based regimens remain an option in areas where these other drugs are not available. Clinical trials are currently underway to evaluate these agents.

Accelerated disease course is the main characteristic of Hepatitis C recurrence after liver transplantation when compared to immunocompetent patients. Approximately one-third of patients will progress to graft cirrhosis within 5 years of the liver transplant. Interferon-based treatments have a poor safety profile and limited efficacy in these patients. There is limited information regarding the treatment of patients with advanced cirrhosis and Hepatitis C after liver transplantation at this time. The presence of significant fibrosis beyond the portal tract (greater than or equal to Metavir F2), portal hypertension (HVPG ≥ 6 mmHG) or high liver stiffness (> 8.7kPa) one year after transplant accurately identify patients with higher risk for clinical decompensation and death. Sofosbuvir and ribavirin for 24 weeks was studied in patients that had a recurrence of HCV (any genotype) at least 6 months after liver transplant. Forty patients received treatment and of these, 28 (70%) achieved SVR12 despite characteristics (treatment-naïve, treatment experienced or compensated cirrhosis). In another study presented at EASL (2014), sofosbuvir plus ribavirin was administered for up to 48 weeks, with patients with compensated and decompensated cirrhosis. SVR12 of 70% was found in patients with acute cholestatic hepatitis/fibrosis cholestatic hepatitis while being 40% in patients with compensated and decompensated cirrhosis.

The AASLD/IDSA recommendations on When and In Whom to Initiate Therapy, updated October 24, 2014, states that, “Successful hepatitis C treatment results in sustained virologic response (SVR), which is tantamount to virologic cure, and as such, is expected to benefit nearly all chronically infected persons. Evidence clearly supports treatment in all HCV-infected persons, except those with limited life expectancy (less than 12 months) due to non-liver related comorbid conditions. Urgent initiation of treatment is recommended in some patients such as those with advances fibrosis and cirrhosis.”

The AASLD/IDSA guidelines recommend that the following should be given the highest priority for treatment based on the highest risk of severe complications:

- Advanced fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4) (Rating Class I, Level A)
- Organ Transplant (Rating Class I, Level B)
- Type 2 or 3 essential mixed cryoglobulinemia and end-organ manifestations (e.g. vasculitis) (Class I, Level B)
- Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis (Class IIa, Level B)

An accurate assessment of fibrosis is vital, in order to determine urgency of treatment. Also as drugs are being FDA approved, many treatment durations are based on the presence or lack of cirrhosis well as degree of liver impairment. Liver biopsy is considered the diagnostic standard with advantages of validated scoring systems, differential diagnosis and associated-conditions and simultaneous evaluation of necro-inflammation. The disadvantages are that liver biopsy is an invasive test that carries come risk along with high cost and the issue of sampling errors due to intra- and inter-observer variability. Non-invasive tests allow for more frequent re-evaluation, less discomfort, objective interpretation and are more acceptable for the patient. They do however have a low accuracy to discriminate between intermediate stages of fibrosis, are not specific for the liver (biomarkers) and are influenced by several hepatic factors. Non-invasive tests to stage the degree of fibrosis are currently being used such as indirect serum biomarkers (routine tests), direct serum biomarkers and vibration-controlled transient liver elastography. No single method is recognized to have high accuracy alone.

Below are commonly used methods to determine degree of fibrosis/cirrhosis for CHC patients:

**METAVIR SCORING:**

Metavir scoring is a fibrosis scale that is graded on a 5-point system from 0 to 4.
**F0** = no fibrosis  
**F1** = portal fibrosis without septa  
**F2** = portal fibrosis with few septa  
**F3** = numerous sept without cirrhosis  
**F4** = cirrhosis

Activity or amount of inflammation (specifically the intensity of necro-inflammatory lesions), is graded on a 4-point scale from A0 to A3.  
**A0** = no activity  
**A1** = mild activity  
**A2** = moderate activity  
**A3** = severe activity

**HCV Fibrosure®**  
Fibrosure is a quantitative test that assess liver fibrosis and attaches a score of 0.00 to 1.00. This range is made to correspond to the Metavir fibrosis score of F0 to F4. It also adds an additional necro-inflammatory score that corresponds to the activity level A0 to A3. It is used in combination with other non-invasive tests to support or rule out the need of liver biopsy. It has also been used to monitor patients with CHC combined with HBV and HIV-1 co-infections. Fibrosure uses components of alanine aminotransferase (ALT), alpha 2-macroglobulin, apolipoprotein A1, total bilirubin, y-glutamyl transferase (GGT), haptoglobin and patient’s age and sex. Corresponding equivalent Metavir scores are listed in the table below as provided from the LabCorp Fibrosure Literature.

<table>
<thead>
<tr>
<th>METAVIR Score</th>
<th>Fibrosis Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0 - no fibrosis</td>
<td>0.00-0.21</td>
</tr>
<tr>
<td>F0-F1</td>
<td>0.21-0.27</td>
</tr>
<tr>
<td>F1 - portal fibrosis</td>
<td>0.27-0.31</td>
</tr>
<tr>
<td>F1-F2</td>
<td>0.31-0.48</td>
</tr>
<tr>
<td>F2 - bridging fibrosis with few septa</td>
<td>0.48-0.58</td>
</tr>
<tr>
<td>F3 - bridging fibrosis with many septa</td>
<td>0.58-0.72</td>
</tr>
<tr>
<td>F3-F4</td>
<td>0.72-0.74</td>
</tr>
<tr>
<td>F4 - cirrhosis</td>
<td>0.74-1.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>METAVIR Score</th>
<th>Activity grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>A0 - no activity</td>
<td>0.00-0.17</td>
</tr>
<tr>
<td>A0-A1</td>
<td>0.17-0.29</td>
</tr>
<tr>
<td>A1 - minimal activity</td>
<td>0.29-0.36</td>
</tr>
<tr>
<td>A1-A2</td>
<td>0.36-0.52</td>
</tr>
<tr>
<td>A2 - moderate activity</td>
<td>0.52-0.60</td>
</tr>
<tr>
<td>A2-A3</td>
<td>0.60-0.63</td>
</tr>
<tr>
<td>A3 - severe activity</td>
<td>0.63-1.00</td>
</tr>
</tbody>
</table>

**INDIRECT BIOMARKERS**  
Serum biomarkers (indirect biomarkers) of fibrosis are general routine tests. The most common ones used in CHC infection include aspartate aminotransferase (AST), alanine aminotransferase (ALT), platelet count, gamma-glutamyltransferase (GGT), bilirubin, haptoglobin, apolipoprotein A1, and alpha-2-macroglobulin.

APRI (AST to Platelet Ratio Index) score is calculated as (AST/upper limit of normal range)/platelet count (10^9/L) × 100. This biomarker is based on the basis that worsening of fibrosis and increased portal pressure
is associated with reduced production of thrombopoietin by hepatocytes, increasing platelet sequestration within the spleen and reduced clearance of AST. Most laboratories use 40 IU/ml as the upper limit of normal range. In a meta-analysis of 40 studies, the best cutoff for diagnosing significant cirrhosis was 0.7 (summary sensitivity 77%, specificity 72%). For detection of cirrhosis, the optimal cutoff score was 1.0 (summary sensitivity 76%, specificity 72%). A score of at least 2 was more specific (91%), but less sensitive (46%). Overall, the APRI score has good diagnostic utility for predicting severe fibrosis/cirrhosis (Metavir F3/F4) or low risk of significant fibrosis, but does not accurately differentiate from mild or severe fibrosis. A major advantage of APRI is that it was tested in HCV/HIV patients in whom overall performance is lower than with mono-infected HCV patients and adjusted cutoffs may increase sensitivity and specificity.

IMAGING TECHNIQUES
Vibration-controlled transient liver elastography is a noninvasive way to measure liver stiffness and does correlate well with measurement of fibrosis. The measurement range does overlap between stages.

- 8.7 kPa correlates with Metavir F2 or higher fibrosis stage
- > 9.5 kPa with Metavir F3
- 14.5 kPa or higher with Metavir 4 or cirrhosis.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- S0146, Injection pegylated interferon alfa-2b, 10mcg
- S0145, Injection pegylated interferon alfa-2a, 180 mcg/mL

REFERENCES

13. Jacobson, et al. Sofosbuvir plus ribavirin achieves high rate of SVR 12 in patients with GT2 or GT3 HCV who were interferon-ineligible, - intolerant, or-unwilling: Results of the phase III POSITRON trial. *NE Virology Issue, June 2013. EASL 2013:61*


POLICY HISTORY

Policy #: 05.01.50
Policy Creation: January 2016
Reviewed: January 2016
Revised: January 2016
Current Effective Date: March 1, 2016

© 2016 Caremark. All rights reserved.