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<th>Prescription Drugs</th>
<th>Effective Date:</th>
<th>January 1, 2021</th>
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<td>Anti-Infective Agents</td>
<td>Original Policy Date:</td>
<td>January 1, 2014</td>
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### Sovaldi Pegasys PegIntron Ribavirin

#### Description

**Sovaldi** (sofosbuvir) with **Pegasys** (peginterferon alfa-2a) or **PegIntron** (peginterferon alfa-2b) and **Ribavirin** (Copegus, Moderiba, Rebetol, RibaPak, Ribasphere, RibaTab, ribavirin)

#### Background

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with hepatitis C virus (HCV) have no symptoms of the disease until liver damage becomes apparent, which may take several years. Some people with chronic HCV infection develop scarring and poor liver function (cirrhosis) over many years, which can lead to complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in the abdomen, infections or liver cancer.

Sovaldi is a nucleotide analog inhibitor that blocks a specific protein needed by the hepatitis C virus to replicate. Sovaldi is to be used as a component of a combination antiviral treatment regimen for certain types of chronic HCV infection. There are several different types of HCV infection. Depending on the type of HCV infection a patient has, the treatment regimen could include Sovaldi and ribavirin or Sovaldi, ribavirin and peginterferon-alfa. Ribavirin and peginterferon-alfa are two drugs also used to treat HCV infection (1).

#### Regulatory Status

FDA-approved indications (1-4):
Sovaldi is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for
the treatment (1):

- Adult patients with genotype 1, 2, 3 or 4 chronic hepatitis C virus (HCV) infection without cirrhosis as a component of a combination antiviral treatment regimen (1).
- Pediatric patients 12 years of age and older or weighing at least 35 kg with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin (1).

Sovaldi should be used in combination with a pegylated interferon and ribavirin for 12 weeks as a therapeutic option for CHC patients with genotype 1 or 4 infection, treatment naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A) (1).

There is a boxed warning for Sovaldi warning about Hepatitis B virus (HBV) reactivation (1).

Pegasys is an antiviral indicated for the treatment of chronic hepatitis C (CHC) in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, in patients with histological evidence of cirrhosis and compensated liver disease, and in adults with CHC/HIV coinfection and CD4 count greater than 100 cells/mm³. Pegasys may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders (2).

PegIntron is an antiviral indicated for the treatment of Chronic Hepatitis C (CHC) in patients with compensated liver disease (3).

There is a boxed warning in regards that PegIntron may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Close monitoring Ribavirin is a nucleoside analogue indicated in combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of Chronic Hepatitis C (CHC) in patients 3 years of age or older with compensated liver disease. When used in combination with ribavirin it may cause birth defects and fetal death; pregnancy in female patient and female partners of male patients should be avoided (3).

Ribavirin is a nucleoside analogue indicated in combination with interferon alfa-2b (pegylated or non-pegylated) for the treatment of Chronic Hepatitis C (CHC) in patients 3 years of age or older with compensated liver disease. Patients with the following characteristics are less likely to benefit from re-treatment after failing a course of therapy: previous nonresponse, previous
pegylated interferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection (3).

Ribavirin has boxed warnings regarding the risk of serious disorders and ribavirin-associated effects. Ribavirin monotherapy is not effective for the treatment of chronic hepatitis; therefore, ribavirin capsules must not be used alone. The primary toxicity of ribavirin is hemolytic anemia. The boxed warning explains that the anemia associated with ribavirin therapy may result in worsening of cardiac disease that has led to fatal and nonfatal myocardial infarctions. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin (4).

There is a boxed warning in regards that ribavirin may cause birth defects and fetal death. Significant teratogenic and embryocidal effects have been demonstrated in all animal species exposed to ribavirin. In addition, ribavirin has a multiple-dose half-life of 12 days, and so it may persist in nonplasma compartments for as long as 6 months. Therefore, ribavirin therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of treatment in both female patients and in female partners of male patients who are taking ribavirin therapy. At least two reliable forms of effective contraception must be utilized during treatment and during the 6-month post treatment follow-up period (4).

The recommended dose of Sovaldi is one 400 mg tablet, taken orally, once daily with or without food. Sovaldi should be used in combination with a pegylated interferon and ribavirin for 12 weeks as a therapeutic option for CHC patients with genotype 1 or 4 infection without hepatocellular carcinomas (1).

No dose recommendation can be given for patients with severe renal impairment (estimated Glomerular Filtration Rate (eGFR) <30 mL/min/1.73m2) or with end stage renal disease (ESRD) due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite (1).

Safety and efficacy of Sovaldi have not been established in patients with decompensated cirrhosis and have not been established in post-liver transplant patients. Available data on subjects with genotype 5 or 6 HCV infection are insufficient for dosing recommendations (1).

If the other agents used in combination with Sovaldi are permanently discontinued, Sovaldi should also be discontinued (1).
Safety and effectiveness of Sovaldi in children less than 18 years of age have not been established (1).

Related policies
Hepatitis C Agents

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Sovaldi in combination with Pegasys/PegIntron and ribavirin may be considered medically necessary in patients 18 years of age or older with chronic Hepatitis C if the conditions indicated below are met.

Sovaldi in combination with Pegasys/PegIntron and ribavirin is considered investigational in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age    18 years of age or older

Diagnosis

Patient must have the following:

Chronic Hepatitis C

AND ALL of the following:
1. Viral genotype 1 or 4
2. Sovaldi will NOT be used as monotherapy
3. Patient does NOT have hepatocellular carcinoma awaiting transplant (these patients should be treated with Sovaldi and ribavirin without interferon)
4. Absence of renal impairment
   a. eGFR must be > 30mL/min/1.73m²
5. Absence of end stage renal disease (ESRD)
6. Patient does NOT have decompensated cirrhosis
7. Patient has NOT had a liver transplant
8. Absence of significant or unstable cardiac disease
9. Neither the patient nor the partner of the patient is pregnant
10. If patient or their partner are of child bearing age, the patient has been or will be instructed to practice effective contraception during therapy and for 6 months after stopping ribavirin therapy
11. NO history of alcohol and/or substance abuse in the past 6 months
12. **Pegasys requests only**: If the patient has a history of Hepatitis B (HBV) infection
   a. Prescriber agrees to monitor for HBV reactivation

**Prior – Approval Renewal Requirements**
None

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**

**Duration**
- Sovaldi 12 weeks (84 tablets for 84 days)
- Pegasys/PegIntron 12 weeks / Ribavirin 12 weeks

**Rationale**

**Summary**
Sovaldi is a nucleotide analog inhibitor that blocks a specific protein needed by the hepatitis C virus to replicate. Depending on the type of HCV infection a patient has, the treatment regimen could include Sovaldi and ribavirin or Sovaldi, ribavirin and peginterferon-alfa. Ribavirin is a nucleoside analogue indicated for the treatment of chronic hepatitis C (CHC) virus infection. Safety and efficacy of Sovaldi have not been established in patients with decompensated cirrhosis and have not been established in post-liver transplant patients. Safety and effectiveness of Sovaldi in children less than 18 years of age have not been established (1-4).
Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Sovaldi, when taken in combination with Pegasys/PegIntron and ribavirin, while maintaining optimal therapeutic outcomes.

References

Policy History

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<th>Date</th>
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<tr>
<td>December 2013</td>
<td>New addition to PA</td>
</tr>
<tr>
<td>March 2014</td>
<td>Annual review</td>
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<tr>
<td>October 2014</td>
<td>Addition of specialist, no alcohol or substance abuse in the last 6 months.</td>
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<td>Addition of Moderiba</td>
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<tr>
<td>March 2015</td>
<td>Annual editorial review and reference update</td>
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<td>December 2015</td>
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<td>Addition of genotype 3</td>
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<tr>
<td>March 2016</td>
<td>Annual editorial review and reference update</td>
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<td>Policy code changed from 5.03.24 to 5.01.24</td>
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<td>December 2017</td>
<td>Annual editorial review and reference update</td>
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<td>Removal of genotype 3</td>
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<tr>
<td>November 2018</td>
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<td>February 2019</td>
<td>Combined with policy 5.01.25 and policy renamed Sovaldi Pegasys PegIntron Ribavirin</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 4, 2020 and is effective on January 1, 2021.