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Section:	Prescription Drugs	**Effective Date:**	January 1, 2019
Subsection:	Anti-Infective Agents	**Original Policy Date:**	January 1, 2014
Subject:	Sovaldi Pegasys Ribavirin	**Page:**	1 of 6

Last Review Date: November 30, 2018

Sovaldi Pegasys Ribavirin

Description

Sovaldi (sofosbuvir) with **Pegasys** (peginterferon alfa-2a) 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 (1).

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 without the need for co-administration of interferon (1).

Regulatory Status
FDA-approved indications: 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 (3). Sovaldi efficacy has been established in subjects with HCV genotype 1, 2, 3, 4 infection, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with

HCV/HIV-1 co-infection (2).

Sovaldi is FDA approved to 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 (2). However, current AASLD/IDSA guidelines do not recommend this regimen as it is considered inferior to current recommended regimens (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/mm^3 . 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 (3).

Ribavirin is a nucleoside analogue indicated for the treatment of chronic hepatitis C (CHC) virus infection (4). 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 (4).

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).

Additionally, Sovaldi has a boxed warning for Hepatitis B virus reactivation, occasionally fulminant, during or after Hepatitis C virus (HCV) therapy which have been reported in HBV/HCV coinfected patients who were not already on HBV suppressive therapy. In light of

these observations, all patients initiating HCV therapy should be assessed for HBV coinfection with testing for HBsAg, anti-HBs, and anti-HBc (2).

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 (2).

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 (2).

If the other agents used in combination with Sovaldi are permanently discontinued, Sovaldi should also be discontinued (2).

Safety and effectiveness of Sovaldi in children less than 18 years of age have not been established (2).

Related policies
Hepatitis C, Olysio, PegIntron, Technivie

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 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 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/1.73m^2
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. 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 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 (1). Ribavirin is a nucleoside analogue indicated for the treatment of chronic hepatitis C (CHC) virus infection (4). 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. Ribavirin therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant. No dose recommendation can be given for patients with severe renal impairment or with end stage renal disease (ESRD). 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 (2).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Sovaldi, when taken in combination with Pegasys and ribavirin, while maintaining optimal therapeutic outcomes.

References

1. AASLD and IDSA: Recommendations for Testing, Managing, and Treating Hepatitis C; May 2018. http://www.hcvguidelines.org. Accessed on August 31, 2018.
2. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
3. Pegasys [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2017.
4. Rebetol capsules [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; October 2017.

Policy History

Date	Action
December 2013	New addition to PA
March 2014	Annual review
October 2014	Addition of specialist, no alcohol or substance abuse in the last 6 months. Addition of Moderiba
March 2015	Annual editorial review and reference update
December 2015	Annual review and reference update

	Addition of genotype 3
March 2016	Annual editorial review and reference update
	Policy code changed from 5.03.25 to 5.01.25
December 2017	Annual editorial review and reference update
	Addition of HBV requirement
November 2018	Annual editorial review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on November 30, 2018 and is effective on January 1, 2019.