RXADVANCE
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Clinical Policy Title:	sofosbuvir
Policy Number:	RxA.483
Drug(s) Applied:	Sovaldi®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Sofosbuvir (Sovaldi®) is hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor.

It is indicated for the treatment of:

- Adult patients with genotype 1, 2, 3 or 4 chronic HCV infection without cirrhosis or with compensated cirrhosis as a component of a combination antiviral treatment regimen.
- Pediatric patients 3 years of age and older with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin (RBV).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Sovaldi®, Ribavirin	Adult patients with chronic HCV infection	Genotype 1: Treatment-naive or treatment-experienced with peg- IFN/RBV patients without cirrhosis: 1 tablet of Sovaldi® 400 mg plus 2 ½ tablets of Ribavirin 200 mg PO OD for 12 weeks	Sovaldi®: 400 mg/day
	Adult patients with chronic HCV infection	Genotype 1 or 4: Treatment-naïve or treatment-experienced, liver transplant patients with or without compensated cirrhosis: 1 tablet of Sovaldi® 400 mg plus 2 ½ tablets of Ribavirin 200 mg PO OD with or without weight-based RBV for 12 weeks	Sovaldi®: 400 mg/day
Sovaldi®, Ribavirin	Adult patients with chronic HCV infection	Genotype 1: Treatment-naïve or treatment-experienced without cirrhosis: 2 ½ tablets of Ribavirin 200 mg plus 1 tablet of Sovaldi® 400 mg PO OD for 12 weeks	Sovaldi®: 400 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Adult patients with chronic HCV infection	Genotype 1, 2, 3, or 4: Decompensated cirrhosis (including those with hepatocellular carcinoma): 2 ½ tablets of Ribavirin 200 mg plus 1 tablet of Sovaldi® 400 mg PO OD with low initial dose of RBV (600 mg) and increased as tolerated	Sovaldi®: 400 mg/day
	Adult patients with chronic HCV infection	Genotype 1, 2, 3, or 4: Decompensated cirrhosis (including those with hepatocellular carcinoma) and intolerant to RBV: 2 ½ tablets of Ribavirin 200 mg plus 1 tablet of Sovaldi® 400 mg PO OD for 24 weeks	Sovaldi®: 400 mg/day
	Adult patients with chronic HCV infection	Genotype 1-6‡: Treatment-naïve or treatment-experienced, post- liver transplantation with or without compensated cirrhosis: 2 ½ tablets of Ribavirin 200 mg plus one tablet of Sovaldi® 400 mg PO OD with low initial dose of RBV (600mg) and increased as tolerated for 12 weeks	Sovaldi®: 400 mg/day
	Adult patients with chronic HCV infection	Genotype 2: Treatment-naïve or treatment-experienced without cirrhosis: 2 ½ tablets of Ribavirin 200 mg plus 1 tablet of Sovaldi® 400 mg PO OD for 12 weeks	Sovaldi®: 400 mg/day
	Adult patients with chronic HCV infection	Genotype 2: Treatment -naïve or treatment- experienced with compensated cirrhosis: 2 ½ tablets of Ribavirin 200 mg plus 1 tablet of Sovaldi® 400 mg PO OD for 16 to 24 weeks	Sovaldi®: 400 mg/day
	Adult patients with chronic HCV infection	Genotype 2 or 3: Treatment-naïve or treatment-experienced, post-liver transplantation with decompensated cirrhosis: 2 ½ tablets of Ribavirin 200 mg plus 1 tablet of Sovaldi® 400 mg	Sovaldi®: 400 mg/day
	Adult patients with chronic HCV	Genotype 3: Treatment-naïve or treatment-	Sovaldi®: 400 mg/day

	infection	experienced with peg IFN/RBV without cirrhosis: 2 ½ tablets of Ribavirin 200 mg plus 1 tablet of Sovaldi® 400 mg PO OD for 12 weeks	
	Adult patients with chronic HCV infection	Genotype 3: Treatment-naïve with compensated cirrhosis: 2 ½ tablets of Ribavirin 200 mg plus one tablet of Sovaldi® 400 mg PO OD with or without weight-based RBV for 24 weeks	Sovaldi®: 400 mg/day
Sovaldi®, Zepatier‡	Adult patients with chronic HCV infection	Genotype 3: pegIFN/RBV-experienced with compensated cirrhosis: Sovaldi® 400 mg PO OD plus Zepatier 1 tablet PO OD for 12 weeks	Sovaldi®: 400 mg per day

AASLD/IDSA treatment guidelines for chronic hepatitis C infection are updated at irregular intervals; refer to the most updated AASLD/IDSA guideline for most accurate treatment regimen.
‡ Off-label, AASLD-IDSA guideline-supported dosing regimen
Treatment-experienced refers to previous treatment with peginterferon/RBV unless otherwise stated
The use of Sovaldi® in combination with peginterferon and ribavirin for the treatment of chronic HCV is no longer recommended by the AASLD/IDSA guidelines.

Drug Name	Indication	Dosing Regimen	Maximum Dose
Sovaldi®, RBV	Pediatric patients (age ≥ 12 years or weighing at least 35 kg) with chronic HCV infection	Genotype 2: Sovaldi® 400 mg + RBV for 12 weeks	Sovaldi®: 400 mg/day
	Pediatric patients (age ≥ 12 years or weighing at least 35 kg) with chronic HCV infection	Genotype 3: Sovaldi® 400 mg + RBV for 24 weeks	Sovaldi®: 400 mg/day

Dosage Forms

- Tablet: 400 mg, 200 mg
- Oral Pellets: 200 mg, 150 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Chronic Hepatitis C Infection (must meet all):

1. Diagnosis of chronic HCV infection as evidenced by detectable serum HCV RNA levels by quantitative assay in the last 6 months;

2. Confirmed HCV genotype is one of the following (a or b):
   a. For adults (≥ 18 years): Genotypes 1, 2, 3, 4, 5, or 6;
   b. For pediatrics (age ≥ 3 years or body weight ≥ 35 kg): Genotypes 2 or 3;
   **Chart note documentation and copies of lab results are required*
3. Documentation of treatment status of the member (treatment-naïve or treatment experienced);
4. Documentation of cirrhosis status of the member (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
5. Prescribed by or in consultation with a gastroenterologist, hepatologist orinfectious disease specialist;
6. Must meet one of the following (a, b, c, or d):
   a. For members ≥ 18 years with genotype 1: Member must use Harvoni® (authorized generic or brand for 8 weeks only), sofosbuvir/velpatasvir (Epclusa®) (authorized generic preferred), Mavyret™, or Zepatier® unless all are contraindicated or clinically significant adverse effects are experienced;
   b. For members ≥ 18 years with genotype 4: Member must use sofosbuvir/velpatasvir (Epclusa®) (authorized generic preferred), Mavyret™, or Zepatier® unless all are contraindicated or clinically significant adverse effectsare experienced;
   c. For members ≥ 18 years with genotype 2, 3, 5, or 6: Member must use sofosbuvir/velpatasvir (Epclusa®) (authorized generic preferred) or Mavyret™, unless all are contraindicated or clinically significant adverse effects are experienced;
   d. For pediatric patients (age ≥ 6 years or weight ≥ 17 kg) with genotype 2 or 3, one of the following (i or ii):
      i. If age between 6 and 11 years, or weight between 17 kg and 44 kg, member must use sofosbuvir/velpatasvir (Epclusa®) (authorized generic preferred), unless are contraindicated or clinically significant adverse effects are experienced
      ii. ii. If age ≥ 12 years or weight ≥ 45 kg: member must use Mavyret™ or sofosbuvir/velpatasvir (Epclusa®) (authorized generic preferred), unless both are contraindicated or clinically significant adverse effects are experienced;
   e. For pediatric patients (age ≥ 3 years) with genotype 1: Member must use Harvoni® (authorized generic or brand for 8 weeks only), unless contraindicated or clinically significant adverse effects are experienced;
7. For pediatric patients (age ≥ 3 years or weight ≥ 35 kg) with genotype 2 or 3: use is in combination with RBV;
8. Life expectancy ≥ 12 months with HCV treatment;
9. Member agrees to participate in a medication adherence program meeting both of the following components (a and b):
   a. Medication adherence monitored by pharmacy claims data or member report;
   b. Member's risk for non-adherence identified by adherence program or member/prescribing physician follow-up at least every 4 weeks;
10. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (see Section V Dosage and Administration for reference);
11. Dose does not exceed 400 mg (1 tablet) per day.

Approval duration

Commercial: for adults: up to a total of 24 weeks & for pedriatics: 12 weeks for genotype 2; 24 weeks for genotype 3

Medicaid: for adults: up to a total of 24 weeks & for pedriatics: 12 weeks for genotype 2; 24 weeks for genotype 3

II. Continued Therapy

A. Chronic Hepatitis C Infection (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Member is currently receiving the medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
   b. Must meet both of the following (i and ii):
      i. Documentation supports that member is currently receiving Sovaldi® for chronic HCV infection and has recently completed at least 60 days of treatment with Sovaldi®;
      ii. Confirmed HCV genotype is one of the following (1 or 2):
         1) For adults (> 18 years): Genotypes 1, 2, 3, 4, 5, or 6;
         2) For pediatrics (age ≥ 3 years or body weight ≥ 35kg): Genotypes 2 or 3;
2. Member is responding positively to therapy;
3. Dose does not exceed 400 mg (1 tablet) per day.

Approval duration

Commercial: for adults: up to a total of 24 weeks & for pedriatics: 12 weeks for genotype 2; 24 weeks for genotype 3

Medicaid: for adults: up to a total of 24 weeks & for pedriatics: 12 weeks for genotype 2; 24 weeks for genotype 3

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
FDA: Food and Drug Administration HBV: hepatitis B virus
HCV: Hepatitis C virus
HIV: Human immunodeficiency virus
RNA: Ribonucleic acid
RBV: Ribavirin
IDSA: Infectious Diseases Society of America

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Harvoni® (sofosbuvir/ ledipasvir)	Without cirrhosis, treatment-naïve, whose HCV viral load is less than 6 million IU/mL: **Genotypes 1** One tablet PO OD for 8	Harvoni: sofosbuvir 400 mg/ ledipasvir 90 mg (1 tablet) per day
Epclusa® (sofosbuvir/ velpatasvir)	Without cirrhosis or with compensated cirrhosis, treatment naïve or treatment experienced: **Genotypes 1 through 6** One tablet PO OD for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Epclusa®	With decompensated cirrhosis (Child-Pugh class B or C) treatment-naïve or treatment	Epclusa: sofosbuvir 400 mg/

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(sofosbuvir/ velpatasvir) plus RBV	experienced: **Genotypes 1 through 6** One tablet PO OD plus weight-based RBV for 12 weeks	velpatasvir 100 mg (1 tablet) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-naïve: **Genotypes 1, 2, 3, 4, 5, or 6** Without cirrhosis: Three tablets PO OD for 8 weeks With compensated cirrhosis: Three tablets PO OD for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: **Genotypes 1, 2, 4, 5, or 6** Without cirrhosis: Three tablets PO OD for 8 weeks With compensated cirrhosis: Three tablets PO OD for12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection: **Genotype 3** Without cirrhosis or with compensated cirrhosis: Three tablets PO OD for 16 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir/ pibrentasvir	Treatment-experienced with NS5A inhibitor without prior NS3/4A protease inhibitor CHC infection: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO OD for 16 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir/ pibrentasvir)	Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor CHC infection: **Genotype 1** Without cirrhosis or with compensated cirrhosis: Three tablets PO OD for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Zepatier®	**Genotype 1a:**	One tablet

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(grazoprevir/ elbasvir)	Treatment-naïve or pegIFN/RBV- experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO OD for 12 weeks	(grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a:** Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO OD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1b:** Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis One tablet PO OD for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a or 1b:** pegIFN/RBV/NS3 PI*‡ -experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO OD plus weight-based RBV for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a or 1b:** pegIFN/RBV/NS3 PI*‡ -experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO OD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 3‡:** pegIFN/RBV-experienced with compensated cirrhosis One tablet PO OD plus sofosbuvir 400 mg for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 4:** Treatment-naïve with or without compensated cirrhosis	One tablet (grazoprevir 100

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	One tablet PO OD for 12 weeks	mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 4:** PegIFN/RBV-experienced with or without compensated cirrhosis with virologic relapse/failure Virologic relapse after prior pegIFN/RBV therapy: One tablet PO OD for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - when used in combination with peginterferon alfa/RBV or RBV alone, all contraindications to peginterferon alfa and/or RBV also apply to Sovaldi® combination therapy.

- Boxed warning(s):
  - risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV

Appendix D: General Information

- Hepatitis B Virus Reactivation (HBV) is a Black Box Warning for all direct-acting antiviral drugs for the treatment of HCV. HBV reactivation has been reported when treating HCV for patients co-infected with HBV, leading to fulminant hepatitis, hepatic failure, and death, in some cases. Patients should be monitored for HBV reactivation and hepatitis flare during HCV treatment and post-treatment follow-up, with treatment of HBV infection as clinically indicated.
- Gane et al. studied 10 patients treated with Sovaldi® monotherapy for 12 weeks who had genotype 2 or 3 disease. The primary efficacy (sustained virologic response (SVR) at 12 weeks after therapy stopped) was much lower (60%) on monotherapy versus 100% on combination therapy.
- Child-Pugh Score:

	1 Point	2 Points	3 Points
Bilirubin	Less than 2 mg/dL Less than 34 umol/L	2-3 mg/dL 34-50 umol/L	Over 3 mg/dL Over 50 umol/L
Albumin	Over 3.5 g/dL Over 35 g/L	2.8-3.5 g/dL 28-35 g/L	Less than 2.8 g/dL Less than 28 g/L
INR	Less than 1.7	1.7 - 2.2	Over 2.2
Ascites	None	Mild/medically controlled	Moderate-severe/ poorly controlled
Encephalopathy	None	Mild/medically controlled Grade I-II	Moderate-severe/ poorly controlled. Grade III-IV

Child-Pugh class is determined by the total number of points: A = 5-6 points; B = 7-9 points; C = 10-15 points.

- The 2017 AASLD/IDSA guidelines no longer recommend Solvadi/RBV for the indication of Genotype 2 or 3

with decompensated cirrhosis (moderate or severe hepatic impairment; CTP class B or C) who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma) or for the indication of hepatocellular carcinoma patients awaiting liver transplantation.

References

1. Sovaldi® Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; March 2020. Available at www.Sovaldi.com. Accessed September 2, 2020.
2. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). HCV guidance: recommendations for testing, evaluation and monitoring of hepatitis C. Last updated August 27, 2020. Available at: https://www.hcvguidelines.org/. Accessed September 2, 2020.
3. Wirth et al. Sofosbuvir-Containing Regimens are Safe and Effective in Adolescents with Chronic hepatitis C Infection. 26th Annual Meeting of the Asian pacific Association forthe Study of the Liver (APASL) on February 15-19, 2017 in Shangahi, China [oralGT1-3]. Accessed September 2, 2020.
4. El-Shabrawi MH, Kamal NM. Burden of pediatric hepatitis C. World J Gastroenterol. 2013 Nov 28;19(44):7880-8. doi: 10.3748/wjg.v19.i44.7880. Accessed September 2, 2020.
5. Wirth S. Current treatment options and response rates in children with chronic hepatitis C. World J Gastroenterol 2012 Jan 14; 18(2): 99-104. doi:10.3748/wjg.v18.i2.99. Accessed September 2, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title table was updated as “1 tablet of Olysio 150 mg and 1 tablet of Daklinza 60 mg were replaced by 2 ½ tablets of Ribavirin 200 mg.” 2. Line of business policies applies to All lines of business. 3. HIM approval duration removed & updated. 4. Dosing Information updated. 5. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by Rxadvance.” 6. References were reviewed and updated.	08/31/2020	12/07/2020