Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCINF029.1225	**ANTI-INFECTIVE AGENTS** **HEPATITIS C DIRECT ACTING ANTIVIRALS** See Table1 for a List of Medications
Effective Date: 2/1/2026	**Review/Revised Date**: 03/16, 05/16, 08/16, 10/16, 12/16, 01/17, 03/17, 07/17, 10/17, 04/18, 11/18, 03/19, 10/19, 10/20, 08/21, 09/21, 10/21, 04/22, 09/22, 11/22, 03/23, 11/23, 02/24, 10/24, 10/25 (JH)
Original Effective Date: 04/16	**P&T Committee Meeting Date**: 04/16, 06/16, 10/16, 12/16, 01/17 (cv), 02/17, 03/17, 08/17, 10/17, 04/18 (cv), 06/18, 12/18, 04/19, 12/19, 12/20, 10/21, 12/21, 04/22, 10/22, 12/22, 04/23, 12/23, 04/24, 10/24, 12/24, 12/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:
Commercial

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-approved indications not otherwise excluded from the benefit.

REQUIRED MEDICAL INFORMATION:
Mavyret® tablet and sofosbuvir/velpatasvir (generic Epclusa) tablet will be covered for patients undergoing solid organ transplantation after confirmation donated solid organ is from a hepatitis C virus (HCV) viremic donor

For all other requests, all the following criteria must be met:
1. Documentation of confirmed diagnosis of chronic hepatitis C virus (HCV) infection (B18.2)
2. Documentation of genotype (tested within the past three years) is only required for the following population:
    a. Patients with cirrhosis
    b. Patients with any prior treatment experience,
    c. For regimens which are not pan-genotypic (e.g., Harvoni®, Zepatier®)
3. Documentation of HCV treatment history and response to therapy. Treatment failure with an NS5A inhibitor due to noncompliance will be reviewed on a case-by-case basis with considerations including, but not limited to, evidence of safety and efficacy, readiness to start therapy, and plan to ensure therapy compliance.
4. Documentation of cirrhosis status. In patients with clinical evidence of liver cirrhosis, Child-Pugh score is required
5. For coverage of non-preferred regimens, the prescriber must submit medical rational in support of its use over formulary alternatives. Coverage of non-

preferred regimens will be reviewed based on evidence and medical necessity over preferred regimens

6. For coverage of oral Harvoni® or Epclusa® pellets, the prescriber must submit medical rational in support of its use over the available generic tablet formulation (such as inability to swallow)

EXCLUSION CRITERIA:
All regimens containing a protease inhibitor (such as Mavyret® and Vosevi®) are not covered in patients with moderate to severe hepatic impairment (Child-Pugh B and C)

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS: N/A

COVERED REGIMEN AND DURATION:
Must be consistent with FDA approved labeling

QUANTITY LIMIT: 28 day-supply per dispense.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Direct acting antiviral (DAA) agents are highly effective oral medications indicated for the treatment of patients infected with chronic hepatitis C infection.

FDA APPROVED INDICATIONS:
Table 1: Preferred and Non-Preferred Direct Acting Antivirals (DAA)[1]

Drug (PI revised date)	FDA Approved Indications
Preferred Agents	

Generic Epclusa - sofosbuvir/ velpatasvir (SOF/VEL) 400/100 mg tablets (04/2022)	Treatment of adult and pediatric patients 3 years of age and older or with chronic HCV genotype (GT) 1, 2, 3, 4, 5, or 6 infections. - Without cirrhosis or with compensated cirrhosis - With decompensated cirrhosis for use in combination with ribavirin
Generic Harvoni - ledipasvir/ sofosbuvir (LED/SOF) 90/400 mg tablet (12/2024)	Treatment of HCV in adults and pediatric patients 3 years of age and older: - GT 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis - GT 1 infection with decompensated cirrhosis, in combination with ribavirin - GT 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin.
Mavyret® (glecaprevir /pibrentasvir) tablet and pellet (06/2025)	Treatment of HCV in adults and pediatric patients 3 years of age and older: - GT 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A). - GT 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both
Vosevi® (sofosbuvir/ velpatasvir/ voxilaprevir) tablet (11/2019)	Treatment of adult patients with HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have: - GT 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor. - GT 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor. ○ Additional benefit of VOSEVI over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.
Non-Preferred Agents	
Sovaldi® (03/2020)	- Adult patients with GT 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 GT 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin
Zepatier® (05/2022)	In combination with or without ribavirin for the treatment of chronic HCV GT 1 or 4 infection in adults and pediatric patients 12 years of age and older or weighing at least 30 kg. Zepatier is indicated for use with ribavirin in certain patient populations
Epclusa® Brand-name tablet/pellet packet	See above
Harvoni® Brand-name tablet/pellet packet	See above

POSITION STATEMENT:

- Chronic hepatitis C infection is a slowly progressive disease. Among patients infected with hepatitis C virus (HCV), 5-20% will go on to develop cirrhosis over a period of 20 to 30 years and 1-5% will die from the consequences of chronic infection.[2]
- The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.[3]
- Drug Resistance Screening Recommendations:
    - Zepatier®: Recommend NS5A resistance testing in HCV genotype 1a-infected patients. Lower SVR12 rates were observed in patients with one or more baseline NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.
- The FDA released a safety communication on 10/4/2016 that warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C. In a few cases, hepatitis B virus (HBV) reactivation in patients treated with DAA medicines resulted in serious liver problems or death.
- The FDA released a safety communication on 8/28/2019 that warns about the use of Mavyret, Zepatier or Vosevi (DAAs that contain protease inhibitor) which have been associated with reports of worsening liver function or liver failure in patients with moderate to severe liver impairment (Child-Pugh B or C).
- Due to the minimal side effect profile and high efficacy of these agents, HCV-infected donor organs are able to be used in transplant procedures with success. Patients receiving these viremic organs may be treated with the DAA therapies and avoid the development of acute hepatitis and other non-hepatic complications.[3]

REFERENCE/RESOURCES:

1. Relevant package labels
2. Centers for Disease Control and Prevention. Viral Hepatitis – Hepatitis C Information. Available at: http://www.cdc.gov/hepatitis/hcv/index.htm
3. American Association for the Study of Liver Disease (AASLD) and Infectious Diseases Society of America (IDSA). Recommendations for testing, managing, and treating hepatitis C. Available at: https://www.hcvguidelines.org/ (Accessed Nov 10, 2025)
4. FDA Drug Safety and Availability [10/4/2016]. “FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C”. Available at:

https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-about-risk-hepatitis-b-reactivating-some-patients-treated

5. FDA Drug Safety and Availability [8/28/2019]. "FDA Drug Safety Communication: FDA warns about rare occurrence of serious liver injury with use of hepatitis C medicines Mavyret, Zepatier, and Vosevi in some patients with advanced liver disease". Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-rare-occurrence-serious-liver-injury-use-hepatitis-c-medicines-mavyret-zepatier-and

Appendix 1: Direct acting antivirals and mechanism of actions

Brand Name	Mechanism of Action		
	NS5A	NS5B	NS3/4A PI
Epclusa	velpatasvir	sofosbuvir	--
Harvoni	ledipasvir	sofosbuvir	--
Mavyret	pibrentasvir	--	glecaprevir
Sovaldi	--	sofosbuvir	--
Vosevi	velpatasvir	sofosbuvir	voxilaprevir
Zepatier	elbasvir	--	grazoprevir