BlueCross BlueShield Arizona

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| **PHARMACY COVERAGE GUIDELINES** | **ORIGINAL EFFECTIVE DATE: 9/15/2016** |
| **SECTION: DRUGS** | **LAST REVIEW DATE: 5/19/2022** |
| | **LAST CRITERIA REVISION DATE: 5/19/2022** |
| | **ARCHIVE DATE:** |

# DIRECT ACTING ANTIVIRAL AGENTS FOR HEPATITIS C VIRUS (HCV): EPCLUSA® (sofosbuvir, velpatasvir) Sofosbuvir with velpatasvir (generic) HARVONI® (ledipasvir, sofosbuvir) Ledipasvir with sofosbuvir (generic) MAVYRET™ (glecaprevir, pibrentasvir) SOVALDI™ (sofosbuvir) VIEKIRA PAK™ (dasabuvir, ombitasvir, paritaprevir, ritonavir) VOSEVI™ (sofosbuvir, velpatasvir, voxilaprevir) ZEPATIER™ (elbasvir, grazoprevir)

**Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.**

**This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.**

**The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.**

**The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.**

**State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.**

**Pharmacy Coverage Guidelines are subject to change as new information becomes available.**

**For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.**



This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

**PHARMACY COVERAGE GUIDELINES**
**SECTION: DRUGS**

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Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

| Hepatitis C Treatment Naive – Oral Agents | | | | | | |
|---|---|---|---|---|---|---|
| | **Genotype 1** | **Genotype 2** | **Genotype 3** | **Genotype 4** | **Genotype 5** | **Genotype 6** |
| **Epclusa** | **X** | **X** | **X** | **X** | **X** | **X** |
| **Harvoni** | **X** | | | **X** | **X** | **X** |
| **Mavyret†** | **X** | **X** | **X** | **X** | **X** | **X** |
| **Sovaldi** | **X** | **X** | **X** | **X** | | |
| **Viekira PAK** | **X** | | | | | |
| **Vosevi** | **X** | **X** | **X** | **X** | **X** | **X** |
| **Zepatier** | **X** | | | **X** | | |
| Harvoni is not FDA approved for genotypes 2,3<br>† No cirrhosis or compensated cirrhosis (Child-Pugh A) | | | | | | |

- **REQUIRED DOCUMENTATION FOR SUBMISSION OF HCV PRIOR AUTHORIZATION REQUESTS**
  For a prior authorization request for HCV medication(s) to be considered, the following minimum information ***must be submitted*** for the member:

1. Assessment for the presence of liver fibrosis and cirrhosis and a determination of whether there is compensated or decompensated liver function
2. A list of previous HCV treatment(s) and the response(s) to these treatment(s)
3. Evidence of Hepatitis A & B vaccinations or laboratory evidence of immunity
4. Testing for other significant viral illnesses must be done within the previous 90 days of the request for treatment of HCV, and if positive, a treatment plan for co-infection therapies must be sent
5. Alcohol and drugs of abuse abstinence contract signed by the patient and provider
6. Results of drug/alcohol screening done within the previous 90 days

7. Results of HCV screening, genotype, and current baseline viral load done within the previous 90 days
8. Results of total bilirubin, albumin, INR, CrCl or GFR, LFTs, CBC done within the previous 90 days
9. Negative pregnancy test in a woman of childbearing potential, unless she is using adequate contraception

**Criteria**:

- **Criteria for therapy:** Epclusa, Harvoni, Mavyret, Sovaldi, Viekira Pak, Vosevi, Zepatier, ledipasvir-sofosbuvir, or sofosbuvir-velpatasvir for **treatment Hepatitis C infection with or without ribavirin** is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist, Hepatologist, or Infectious Disease provider
2. Individual age (and weight, where appropriate) is consistent with the FDA-label
3. A confirmed diagnosis of chronic hepatitis C virus (HCV)
4. Individual with past hepatitis C treatment has been compliant with previous and/or current drug therapy
5. There must be no alcohol and/or no substance use in the past 6 months
6. There are **NO** FDA-label contraindications for use of agent(s) requested
7. There are no significant interacting drugs
8. **For Sovaldi, Viekira Pak, Vosevi, Zepatier, generic ledipasvir with sofosbuvir, or generic sofosbuvir with velpatasvir:** Failure, contraindication per FDA label, intolerance to **at least 2** of the following agents:
    a. Epclusa
    b. Harvoni
    c. Mavyret
9. **For HCV treatment requiring concurrent use of ribavirin and the individual is not currently on ribavirin**: Failure, contraindication per FDA label, intolerance to **generic ribavirin 200mg**
10. Requested treatment regimen is consistent with product labeling, current clinical guideline recommendation from AASLD / IDSA for the specific HCV genotype, liver evaluation, treatment status, prior treatment history, and comorbidities

**Approval duration:** Per HCV genotype and patient specific factors
Prescribing provider must submit viral load after 12 weeks of completion of therapy (SVR12)

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

**Description:**

The presence of hepatitis C (HCV) antibody and HCV RNA are used to support a diagnosis of HCV infection. There are at least six major genotypes and several subtypes of HCV. Baseline viral load by quantitative assay and genotype are necessary to guide therapeutic options.

Hepatitis C infection is a major cause of chronic liver disease and a leading reason for liver transplantation. Sequelae of chronic hepatitis may include liver fibrosis, cirrhosis, liver failure, and hepatocellular carcinoma. Hepatocellular carcinoma rarely progresses without underlying fibrosis and cirrhosis.

During acute HCV infection, there is a 20-50% chance of spontaneous resolution of infection. In at least two-thirds of individuals, this will occur within 6 months of the estimated time of infection; only 11% of those who remain viremic at 6 months will spontaneously clear infection at some time later.

Treatment of HCV is rapidly evolving, and clinical practice guidelines change as new agents and results of clinical studies become available. Newer agents alone or used in combination with other agents attempt to improve sustained virologic response (SVR) rates, reduce pill-burden, reduce drug-drug interactions, and improve patient tolerance to the medication. The American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) jointly publish a guideline on the treatment of HCV that can be accessed at http://www.hcvguidelines.org/full-report-view. The guideline has recommendations for testing, managing, and treating all HCV genotypes. Treatment options should consider patient-specific factors such as HCV genotype, prior treatment history, presence or absence of compensated or decompensated cirrhosis. The guidance uses evidence-based information.

Ribavirin in combination with an interferon or non-interferon oral anti-hepatitis C antiviral medications is indicated for the treatment of chronic hepatitis C viral (HCV) infection in patients with compensated liver disease. Ribavirin is a synthetic nucleoside analog (purine analog) with antiviral activity. It inhibits replication of RNA and DNA viruses; it inhibits influenza virus RNA polymerase activity and it inhibits the initiation and elongation of RNA fragments resulting in inhibition of viral protein synthesis.

HCV is an RNA virus that utilizes several important enzymes for reproduction. One is a NS3/4A serine protease enzyme that acts to cut large HCV encoded proteins into smaller pieces that are used to build new viruses. It is essential for viral replication. An additional enzyme that is essential for viral replication is NS5B RNA-dependent RNA polymerase that synthesizes the viral genome. The RNA polymerase initiates RNA synthesis by forming a bond between nucleotides that also begins the elongation process of RNA synthesis. A third enzyme, NS5A functions through interaction with other NS viral proteins and other cellular proteins that play a role in mediating

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host cell function and HCV viral replication, assembly, and egress Cross-resistance is possible between HCV NS3/4A protease inhibitors and between HCV NS5A inhibitors by class.

About 10-15% of HCV genotype 1 infected patients without prior exposure to NS5A inhibitors will have detectable HCV NS5A resistance associated substitutions (RASs) prior to treatment. The presence of baseline NS5A RASs can cause a large reduction in the activity (> 5-fold) of NS5A inhibitors that potentially adversely impact response to NS5A containing regimens. Given that baseline NS5A RASs are one of the strongest pretreatment predictors of treatment outcome with certain regimens, testing for these RASs prior to deciding on a therapeutic course is now recommended in select situations. Patients with genotype 1a may have higher rates of failure than genotype 1b and RASs testing is recommended for genotype 1a. If the genotype cannot be subtyped recommendations from AASLD is to treat as a genotype 1a infection.

**Definitions:**

**Per FDA-label, indicated age of:**

- 18 years of age or older for Viekira Pak, Vosevi, and Zepatier
- 12 years of age or older for Mavyret
- 6 years of age or older for Epclusa and generic sofosbuvir-velpatasvir
- 3 years of age or older for Harvoni, generic ledipasvir-sofosbuvir, and Sovaldi

**Direct acting antiviral agents for hepatitis C, oral:**

***NS3/4A serine protease inhibitors:***

Glecaprevir – found in Mavyret
Grazoprevir – found in Zepatier
Paritaprevir – found in Viekira Pak
Voxilaprevir – found in Vosevi

***NS5A inhibitors:***

Elbasvir – found in Zepatier
Ledipasvir – found in Harvoni
Ombitasvir – found in Viekira Pak
Pibrentasvir – found in Mavyret
Velpatasvir – found in Epclusa, Vosevi

***NS5B polymerase inhibitors:***

Dasabuvir – non-nucleoside inhibitor found in Viekira Pak
Sofosbuvir – nucleotide inhibitor found in Sovaldi, Harvoni, Epclusa, and Vosevi

***CYP3A inhibitors:***

Ritonavir – inhibitor of metabolism, found in Viekira Pak

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**The Child-Pugh classification system:**

The Child-Pugh classification is a scoring system used to determine the prognosis of chronic liver disease and cirrhosis. Scoring is based upon several factors: albumin, total bilirubin, prothrombin time or international normalized ratio, and degrees of ascites and encephalopathy

| Child-Pugh Classification of severity of liver disease | | | |
|---|---|---|---|
| Child-Pugh Classification | Points | | |
| A: Well compensated | 5-6 | | |
| B: Significant functional compromise | 7-9 | | |
| C: Decompensated | 10-15 | | |
| | | | |
| Parameter/Factor | 1 point each | 2 points each | 3 points each |
| Total Bilirubin, mg/dL (or µmol/L) | < 2 (or < 34) | 2-3 (or 34-50) | >3 or (> 50) |
| Albumin, g/dL (or g/L) | >3.5 (or > 35) | 2.8-3.5 (or 28-35) | < 2.8 (or < 28) |
| Prothrombin time prolongation: | | | |
| Seconds over control | 1-3 | 4-6 | > 6 |
| INR | < 1.7 | 1.71-2.3 | > 2.3 |
| Ascites | Absent | Slight/Mild | Moderate to severe |
| Encephalopathy | None | Grade 1-2 (or suppressed with medication) | Grade 3-4 (or refractory) |

**Ribavirin intolerance or ineligibility – requirements**

Platelets < 50,000 cell/$mm^3$
Neutrophils < 750 cell/$mm^3$
Hemoglobin < 10 g/dL
Autoimmune hepatitis or other autoimmune condition known to be exacerbated by ribavirin
Pregnancy
Hemoglobinopathies
Creatinine clearance less than 50 mL/min
Coadministration with didanosine
Known hypersensitivity reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme)

**Resources:**

Epclusa (velpatasvir-sofosbuvir) product information, revised by Gilead Sciences, Inc. 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 22, 2022.

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