



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 9/15/2016
LAST REVIEW DATE: 5/21/2020
LAST CRITERIA REVISION DATE: 5/21/2020
ARCHIVE DATE:

DIRECT ACTING ANTIVIRAL AGENTS FOR HEPATITIS C VIRUS (HCV):

DAKLINZA™ (daclatasvir) oral tablet

EPCLUSA® (sofosbuvir, velpatasvir) oral tablet

HARVONI® (ledipasvir, sofosbuvir) oral tablet and pellets

MAVYRET™ (glecaprevir, pibrentasvir) oral tablet

OLYSIO™ (simeprevir sodium) oral capsule

SOVALDI™ (sofosbuvir) oral tablet

TECHNIVIE™ (ombitasvir, paritaprevir, ritonavir) oral tablet

VIEKIRA PAK™ (dasabuvir, ombitasvir, paritaprevir, ritonavir) oral tablet therapy pack

VIEKIRA XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir) extended release oral tablet

VOSEVI™ (sofosbuvir, velpatasvir, voxilaprevir) oral tablet

ZEPATIER™ (elbasvir, grazoprevir) oral tablet

Ledipasvir, sofosbuvir oral tablet

Sofosbuvir, velpatasvir oral tablet

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.

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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.

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 – Preferred 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

Harvoni is not FDA approved for genotypes 2,3
† No cirrhosis or compensated cirrhosis (Child-Pugh A)

REQUIRED DOCUMENTATION FOR SUBMISSION OF HCV PRIOR AUTHORIZATION REQUESTS

In order for a prior authorization request for HCV medications to be considered, the following minimum information must be submitted for the member:

1. Evaluation 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 treatments and responses to therapy
3. Evidence of Hepatitis A & B vaccinations or laboratory evidence of immunity
4. Testing for other significant viral illnesses must be done within 90 days of request for treatment of HCV, if positive, a treatment plan for co-infection therapies must be sent
5. There must be a drugs of abuse and alcohol abstinence contract signed by the patient and provider
6. Laboratory results for and drug/alcohol screen completed within the past 90 days
7. Laboratory results HCV screen, genotype and current baseline viral load within last 90 days



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8. Laboratory results for total bilirubin, albumin, INR, CrCl or GFR, LFTs, CBC within past 90 days
9. There must be a negative pregnancy test in a woman of child bearing potential, unless she is using adequate contraception

Criteria:

- **Criteria for therapy:** Daklinza, Epclusa, Harvoni, Mavyret, Olysio, Sovaldi, Technivie, Viekira Pak, Viekira XR, Vosevi, Zepatier, ledipasvir-sofosbuvir, and 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 is **ONE** of the following:
 - 18 years of age or older for Daklinza, Olysio, Technivie, Viekira Pak, Viekira XR, Vosevi, and Zepatier
 - 12 years of age or older for Mavyret and Sovaldi
 - 6 years of age or older for Epclusa and sofosbuvir-velpatasvir
 - 3 years of age or older for Harvoni and ledipasvir-sofosbuvir
 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 must be no contraindications for use of agent(s) requested
 7. There are no significant interacting drugs
 8. For **non-preferred** drugs: Failure, contraindication or intolerance to **at least 2** of the preferred agents (See Table) by HCV genotype, liver evaluation, and treatment history
 9. For **HCV treatment requiring concurrent use of ribavirin and the individual is not currently on ribavirin**: Failure, contraindication or 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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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 progress 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 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

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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:

Direct acting antiviral agents for hepatitis C, oral:

NS3/4A serine protease inhibitors:

- Boceprevir – found in Victrelis, no longer available on the market
- Glecaprevir – found in Mavyret
- Grazoprevir – found in Zepatier
- Paritaprevir – found in Viekira Pak, Viekira XR, and Technivie
- Simeprevir – found in Olysio
- Telaprevir – found in Incivek, no longer available on the market
- Voxilaprevir – found in Vosevi

NS5A inhibitors:

- Daclatasvir – found in Daklinza
- Elbasvir – found in Zepatier
- Ledipasvir – found in Harvoni
- Ombitasvir – found in Viekira Pak, Viekira XR, and Technivie
- Pibrentasvir – found in Mavyret
- Velpatasvir – found in Epclusa, Vosevi

NS5B polymerase inhibitors:

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

CYP3A inhibitors:

- Ritonavir – inhibitor of metabolism, found in Viekira Pak, Viekira XR, and Technivie

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



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	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)

HCV treatment options by genotype:

	FDA-Approved indications					
	Genotype 1	Genotype 2	Genotype 3	Genotype 4	Genotype 5	Genotype 6
Daklinza + Sovaldi ± RBV	X		X			
Eplclusa (brand and generic)	X	X	X	X	X	X
Harvoni (brand and generic)	X			X	X	X
Mavyret†	X	X	X	X	X	X
Olysio* + RBV / Peg-INF	X			X		
Olysio* + Sovaldi	X					
Sovaldi + RBV / Peg-INF	X			X		
Sovaldi + RBV		X	X			
Technivie + RBV				X		
Viekira Pak ± RBV & Viekira XR ± RBV	X					
Vosevi†	X*	X	X*	X	X	X
Zepatier**	X			X		

† It is indicated for treatment-naïve genotype 1-6 patients without cirrhosis or with compensated cirrhosis (C-P Class A) and also indicated for genotype 1 patients without cirrhosis or with compensated cirrhosis (C-P Class A) previously treated for HCV infection with a regimen that contained NS3/4A protease inhibitor or NS5A inhibitor, but not both and for genotypes 1-6 previously treated with pegylated interferon, ribavirin, and/or sofosbuvir, but no prior NS3/4 or NS5A inhibitors

* No Q80K substitution

+ It is indicated for individuals previously treated a HCV regimen: for genotypes 1-6 without cirrhosis or with compensated cirrhosis (C-P Class A) whose previous regimen contained a NS5A inhibitor and for genotype 1a or 3 whose regimen contained sofosbuvir without an NS5A inhibitor

** No baseline NS5A RASs at amino acid positions M28, Q30, L31, and Y93 for genotype 1a

Duration of treatment, depending on regimen, can be as short as 8 weeks but usually ranges 12-24 weeks, and is influenced by genotype, agent(s) selected, prior treatment, presence of compensated or decompensated cirrhosis, and other patient specific factors

RBV = Ribavirin

Peg-INF = pegylated interferon

Ribavirin intolerance or ineligibility – requirements

Platelets < 50,000 cell/mm³

Neutrophils < 750 cell/mm³

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



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Known hypersensitivity reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme)

Resources:

Epclusa (sofosbuvir-velpatasvir) product information accessed 04-04-20 at DailyMed

Sofosbuvir-velpatasvir product information accessed 04-06-20 at DailyMed

Harvoni (ledipasvir-sofosbuvir) product information accessed 04-04-20 at DailyMed

Ledipasvir-sofosbuvir product information accessed 04-06-20 at DailyMed

Mavyret (glecaprevir-pibrentasvir) product information accessed 04-04-20 at DailyMed

Sovaldi (sofosbuvir) product information accessed 04-04-20 at DailyMed

Viekira Pak (dasabuvir-ombitasvir-paritaprevir-ritonavir) product information accessed 04-04-20 at DailyMed

Vosevi (sofosbuvir-velpatasvir-voxilaprevir) product information accessed 04-04-20 at DailyMed

Zepatier (elbasvir-grazoprevir) product information accessed 04-04-20 at DailyMed

Ribavirin product information accessed 04-04-20 at DailyMed

Daklinza (daclatasvir) product information accessed 04-04-20 at DailyMed

Olysio (simeprevir) product information accessed 04-04-20 at DailyMed

Technivie (ombitasvir-paritaprevir-ritonavir) product information accessed 04-04-20 at DailyMed

Viekira XR (dasabuvir-ombitasvir-paritaprevir-ritonavir) product information accessed 04-04-20 at DailyMed

Rebetol product information accessed 04-04-20 at DailyMed

Mavyret. Package insert. Revised by manufacturer 8/2017.

Vosevi. Package insert. Revised by manufacturer 7/2017.

Daklinza. Package Insert. Revised by manufacturer 4/2016.

Epclusa. Package Insert. Revised by manufacturer 6/2016.



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Harvoni. Package Insert. Revised by manufacturer 6/2016.

Olysio. Package Insert. Revised by manufacturer 5/2016.

Sovaldi. Package Insert. Revised by manufacturer 8/2015.

Technivie. Package Insert. Revised by manufacturer 6/2016.

Viekira Pak. Package Insert. Revised by manufacturer 6/2016.

Viekira XR. Package Insert. Revised by manufacturer 7/2016.

Rebetol. Package Insert. Revised by manufacturer 1/2016.

Zepatier. Package Insert. Revised by manufacturer 1/2016.

AASLD/IDSA/IAS–USA. Recommendations for Testing, Managing, and Treating Hepatitis C.
<http://www.hcvguidelines.org>. Accessed Oct. 14, 2014

Afdhal N, Reddy KR, Nelson DR et al. Ledipasvir and Sofosbuvir for Previously Treated HCV Genotype 1 Infection. NEJM April 17, 2014 370; 16: 1483-1493

Kowdley KV, Gordon SV, Reddy KR et al. Ledipasvir and Sofosbuvir for 8 or 12 Weeks for Chronic HCV without Cirrhosis NEJM May 15, 2014 370; 19:1879-1888

WHO Guidelines for treatment of hepatitis C <http://www.who.int/mediacentre/factsheets/fs164/en/> Accessed 10/27/14

UpToDate: Overview of the management of chronic hepatitis C virus infection. Current through Aug 2017

Copegus. Package Insert. Revised by manufacturer 08-2015. Accessed 01-09-2018.

Moderiba. Package Insert. Revised by manufacturer 12-2017. Accessed 01-09-2018.

Rebetol. Package Insert. Revised by manufacturer 01-2016. Accessed 01-09-2018.

Ribasphere. Package Insert. Revised by manufacturer 12-2015. Accessed 07-09-2018.

Ribavirin. Package Insert. Revised by manufacturer 01-2016. Accessed 01-09-2018.

UpToDate: Ribavirin (systemic): Drug information