Treatment of Hepatitis C with sofosbuvir/velpatasvir (Epclusa®, Authorized Generic)

Policy # 00514
Original Effective Date: 08/17/2016
Current Effective Date: 11/11/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Treatment of Hepatitis C with Dual Therapy (Ribavirin Plus Pegylated Interferon Alfa) is addressed separately in medical policy 00374.

Note: Pegylated Interferons (Pegasys®, PegIntron®) for Other (Non-Hepatitis C) Uses is addressed separately in medical policy 00375.

Note: Treatment of Hepatitis C with a sofosbuvir (Sovaldi®) Based Regimen is addressed separately in medical policy 00397.

Note: Treatment of Hepatitis C with ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak®) is addressed separately in medical policy 00462.

Note: Treatment of Hepatitis C with elbasvir and grazoprevir (Zepatier™) is addressed separately in medical policy 00509.

Note: Treatment of Hepatitis C with sofosbuvir/ledipasvir (Harvoni®, Authorized Generic) is addressed separately in medical policy 00455.

Note: Treatment of Hepatitis C with glecaprevir/pibrentasvir (Mavyret™) is addressed separately in medical policy 00593.

Note: Treatment of Hepatitis C with sofosbuvir/velpatasvir/voxilaprevir (Vosevi™) is addressed separately in medical policy 00594

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When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Branded Epclusa Requests

Based on review of available data, the Company may consider sofosbuvir/velpatasvir (Epclusa®)‡ for the treatment of individuals with chronic hepatitis C virus (HCV) to be **eligible for coverage.****

Patient Selection Criteria

Based on review of available data, the Company may consider sofosbuvir/velpatasvir (Epclusa) for the treatment of HCV when the following criteria are met:

- Patient has a diagnosis of chronic hepatitis C virus (HCV) genotypes 1, 2, 3, 4, 5, or 6; AND
- Patient has NOT failed prior therapy with drugs such as elbasvir/grazoprevir (Zepatier™)‡, sofosbuvir/ledipasvir (Harvoni®‡, Authorized Generic), sofosbuvir/velpatasvir (Epclusa, Authorized Generic), ombitasvir, paritaprevir, ritonavir, dasabuvir (Viekira Pak/XR®)‡, daclatasvir (Daklinza™)‡, sofosbuvir (Sovaldi®)‡, glecaprevir/pibrentasvir (Mavyret™)‡, sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)‡, or ombitasvir, paritaprevir, ritonavir (Technivie®)‡; AND
- Patient meets the following definitions and adheres to the timeframes for treatment (including concomitant medications):

Patient Population	Recommended Treatment Regimen
Treatment naïve and treatment experienced[1] withOUT cirrhosis and with compensated cirrhosis (Child Pugh A)	Epclusa for 12 weeks
Treatment naïve and treatment experienced[1] with decompensated cirrhosis (Child Pugh B and C)	Epclusa PLUS ribavirin for 12 weeks
Liver Transplant Recipients: Treatment naïve and treatment experienced[1] withOUT cirrhosis and with compensated cirrhosis (Child Pugh A)	Epclusa for 12 weeks

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[1]Patients in trials were treatment experienced with peginterferon/ribavirin OR peginterferon/ribavirin plus a protease inhibitor (Incivek, Victrelis, Olysio).

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of sofosbuvir/velpatasvir (Epclusa) when patient selection criteria are not met to be **investigational.***

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Epclusa Quantity Override

Based on review of available data, the Company may consider a quantity override for the "non-standard" dosage forms (e.g., dosage forms other than the 400 mg/100 mg tablets) of sofosbuvir/velpatasvir (Epclusa) for the treatment of pediatric patients with chronic hepatitis C virus (HCV) to be **eligible for coverage.****

Patient Selection Criteria

Based on review of available data, the Company may consider a quantity override for the "non-standard" dosage forms (e.g., dosage forms other than the 400 mg/100 mg tablets) of sofosbuvir/velpatasvir (Epclusa) for pediatric patients when the following criterion is met:

- Patient meets the criteria for sofosbuvir/velpatasvir (Epclusa) approval; AND
- A valid clinical reason exists as to why the patient cannot take ONE unit of a dosage form daily versus TWO units of a dosage form daily.
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers use of the "non-standard" dosage forms (e.g., dosage forms other than the 400 mg/100 mg tablets) of sofosbuvir/velpatasvir (Epclusa) for the treatment of pediatric patients with chronic hepatitis C virus (HCV) when NO valid clinical reason exists as to why the patient cannot take ONE unit of a dosage form daily versus TWO units of a dosage form daily to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review on available data, the Company considers use of the "non-standard" dosage forms (e.g., dosage forms other than the 400 mg/100 mg tablets) of sofosbuvir/velpatasvir (Epclusa) in adults to be **investigational.***

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

sofosbuvir/velpatasvir Authorized Generic Requests

Based on review of available data, the Company may consider the sofosbuvir/velpatasvir authorized generic for the treatment of individuals with chronic hepatitis C virus (HCV) to be **eligible for coverage.****

Patient Selection Criteria

Based on review of available data, the Company may consider the sofosbuvir/velpatasvir authorized generic when the following criteria are met:

- Patient meets the criteria for sofosbuvir/velpatasvir (Epclusa) approval; AND

- There is clinical evidence or patient history that suggests the use of the clinically applicable preferred products [i.e., sofosbuvir/velpatasvir (Epclusa), sofosbuvir/ledipasvir (Harvoni)] be ineffective or will cause an adverse reaction to the patient.
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of the sofosbuvir/velpatasvir authorized generic when there is an absence of clinical evidence or patient history that suggests the use of the clinically applicable preferred products [i.e., sofosbuvir/velpatasvir (Epclusa), sofosbuvir/ledipasvir (Harvoni)] will be ineffective or will cause an adverse reaction to the patient to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of the sofosbuvir/velpatasvir authorized generic when the criteria for the parent drug, Epclusa, would have been denied as **investigational*** to be **investigational.***

Background/Overview

Epclusa is a combination of two products: sofosbuvir, a HCV nucleotide analog NS5B polymerase inhibitor, and velpatasvir, a HCV NS5A inhibitor, approved for the treatment of adult patients and pediatric patients 3 years of age and older with chronic HCV genotypes 1, 2, 3, 4, 5, or 6 infection. This includes treatment naïve and treatment experienced liver transplant recipients without cirrhosis or with compensated cirrhosis. Various dosage forms now exist for Epclusa. There are tablets containing 400 mg of sofosbuvir and 100 mg of velpatasvir as well as tablets containing 200 mg of sofosbuvir and 50 mg of velpatasvir. There are also oral pellets containing 200 mg of sofosbuvir and 50 mg of velpatasvir as well as oral pellets containing 150 mg of sofosbuvir and 37.5 mg of velpatasvir. Refer to the package insert for specific dosing based on age and body weight. However, note that the 400 mg/100 mg tablets are intended for adults and certain pediatric patients only.

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The "non-standard" dosage forms (dosage forms other than the 400 mg/100 mg tablets) are intended for pediatric patients only. In some instances, the package insert recommends taking two lower strength dosage forms to equal one higher strength dosage form, which is already commercially available. These requests will be reviewed for clinical reasoning as to why one dosage form unit cannot be used versus the two units.

In early 2019, Asegua Therapeutics, a subsidiary of Gilead, launched an authorized generic of Epclusa, which carries the same indications. The ingredients in the authorized generic product are identical to Epclusa.

Hepatitis C
Hepatitis C is the most common blood borne pathogen. In the US, there are approximately 5.2 million people chronically infected with hepatitis C. Hepatitis C, a single-stranded ribonucleic acid (RNA) virus, is genetically complex with several recognized genotypes. Genotypes 1, 2, and 3 are the most frequently encountered genotypes worldwide.

Drug regimens have evolved quite a bit over the past few years in this class. It is beyond the scope of this policy to delve into the entire timeline of approvals, however a brief overview will provide an idea of the evolution of these drugs. The earlier regimens contained ribavirin and interferon/pegylated interferons. The next wave of products brought NS3/4A protease inhibitors to market such as Incivek®‡ and Victrelis®‡. After that, an NS5B polymerase inhibitor was approved (Sovaldi). Following the release of Sovaldi, a drug was approved that contained a combination NS5A inhibitor and NS5B polymerase inhibitor combination (Harvoni). Drugs approved up until that point in time mainly treated genotype 1 hepatitis C virus. After these drugs were approved, a multitude of other drugs were approved (Viekira/XR, Zepatier, Daklinza, etc). As drugs continue to be FDA approved in this space, the range of genotypes that can be treated increases. The latest wave of drugs includes pangenotypic products such as Eplcusa, Mavyret, and Vosevi. For more information on each individual drug, please see the product's package insert or refer to their respective medical policy.

Epclusa has been integrated into the American Association for the Study of Liver Diseases (AASLD) guidelines in various scenarios for the treatment of HCV, however it should be noted that these guidelines are receiving constant updates as new products are approved.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Epclusa was approved in June of 2016 for the treatment of adult patients with chronic HCV genotypes 1, 2, 3, 4, 5, and 6. The authorized generic of Epclusa was launched in early 2019 with identical indications to the parent drug. In 2020, Epclusa was approved for use in pediatric patients aged 6 years and older. The package insert was also updated at this time to include treatment naïve and treatment experienced liver transplant recipients without cirrhosis or with compensated cirrhosis. In 2021, the age expanded to those 3 years of age and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

With/Without Compensated Cirrhosis

ABSTRAL-1 was a randomized, double-blind, placebo-controlled trial that evaluated 12 weeks of treatment with Epclusa vs. 12 weeks of placebo in subjects with genotype 1, 2, 4, 5, or 6 HCV infection. Subjects in this study either had no cirrhosis or had compensated cirrhosis. The overall SVR12 for all genotypes was 99%. For genotype 1, the SVR was 98%, for genotype 2, 100%, genotype 4, 100%, genotype 5, 97%, and genotype 6 was 100%. In this trial, there were no on-treatment virologic failures and <1% relapses.

ABSTRAL-2 was a randomized, open-label trial that evaluated 12 weeks of therapy with Epclusa versus treatment with Sovaldi plus ribavirin in patients with genotype 2 HCV. This study included those that were both treatment naïve and treatment experienced. This trial also included subjects

without cirrhosis or with compensated cirrhosis. The SVR12 in the Epclusa group was 99% versus 94% in the Sovaldi plus ribavirin group. There were no on-treatment virologic failures in either groups. There were no relapses in the Epclusa group versus 5% of the population relapsing in the Sovaldi plus ribavirin group.

ABSTRAL-3 was a randomized, open-label trial that studied 12 weeks of Epclusa versus 24 weeks of Sovaldi plus ribavirin in patients with genotype 3 HCV. There were both treatment naïve and treatment experienced subjects in this trial. This trial also included subjects without cirrhosis or with compensated cirrhosis. The SVR12 in this Epclusa group was 95% versus 80% in the Sovaldi plus ribavirin group. There were no on-treatment virologic failures in the Epclusa group versus <1% in the Sovaldi plus ribavirin group. There was a 4% relapse rate in the Epclusa group versus a 14% rate in the Sovaldi plus ribavirin group.

DEcompensated Cirrhosis

ABSTRAL-4 was a randomized, open-label trial in subjects with genotypes 1, 2, 3, 4, 5, or 6 with decompensated cirrhosis. Subjects were randomized to Epclusa for 12 weeks or Epclusa plus ribavirin for 12 weeks or Epclusa for 24 weeks. The Epclusa plus ribavirin regimen had numerically higher SVR rates than the other two regimens. The overall SVR12 for all genotypes was 94% with a 3% virologic failure rate.

Pediatrics

The efficacy of Epclusa once daily for 12 weeks was evaluated in an open-label trial in genotype 1, 2, 3, 4, or 6 HCV treatment-naïve or treatment-experienced pediatric subjects 3 years of age and older without cirrhosis or with compensated cirrhosis. In subjects 12 to less than 18 years of age, the SVR 12 was 93% in subjects with genotype 1 HCV and 100% in genotypes 2, 3, 4, and 6. In subjects 6 years to less than 12 years, the SVR12 was 93% in subjects with genotype 1 HCV, 91% in subjects with genotype 3 HCV and 100% in genotypes 2 and 4 HCV. In subjects 3 years to less than 6 years of age, the SVR12 was 88% in subjects with genotype 1 HCV, 50% in genotype 2 HCV, and 100% in genotypes 3 and 4.

References

1. Epclusa [package insert]. Gilead Sciences, Inc. Foster City, California. Updated June 2021.
2. Recommendations for Testing, Managing, and Treating Hepatitis C. American Association for the Study of liver diseases. Updated January 2021.
3. Sofosbuvir/velpatasvir [package insert]. Asegua Therapeutics. Foster City, California. Updated June 2021.

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Policy History

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08/04/2016	Medical Policy Committee review
08/17/2016	Medical Policy Implementation Committee approval. New Policy.
08/03/2017	Medical Policy Committee review
08/23/2017	Medical Policy Implementation Committee approval. No change to coverage.
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Removed the requirement for Harvoni first prior to Epclusa for genotypes 1, 4, 5, 6. Updated background info.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. No change to coverage.
08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. Added the authorized generic of Epclusa to the policy. Updated relevant sections with coverage criteria and background information.
08/06/2020	Medical Policy Committee review
08/12/2020	Medical Policy Implementation Committee approval. No change to coverage.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. Updated the policy to include pediatric information and information about new dosage forms and strengths. Included a quantity override to go along with the new strengths. Combined all genotypes into one patient selection section to more closely resemble the package insert and treatment guidelines.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. Removed Mavyret as an option to use prior to the authorized generic of Epclusa. Included liver transplant recipients for clarity purposes in the treatment box.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. No change to coverage.
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. No change to coverage.

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10/03/2024 Medical Policy Committee review
10/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 10/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.