# Clinical Policy: Ledipasvir/Sofosbuvir (Harvoni)

Reference Number: HIM.PA.SP3
Effective Date: 08.01.16
Last Review Date: 06.18
Line of Business: HIM

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

Ledipasvir/sofosbuvir (Harvoni®) is a fixed-dose combination of ledipasvir, a hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor.

## FDA Approved Indication(s)

Harvoni is indicated for the treatment of chronic HCV in:

- Adults with genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
- Adults with genotype 1 infection with decompensated cirrhosis, in combination with ribavirin
- Adults with genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin
- Pediatric patients 12 years of age and older or weighing at least 35 kg with genotype 1, 4, 5, or 6 without cirrhosis or with compensated cirrhosis

## Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Harvoni is **medically necessary** when the following criteria are met:

**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 1, 4, 5 or 6;
   **Chart note documentation and copies of lab results are required*
3. For treatment-naïve adult members with genotype 1, documentation of baseline viral load;
4. Documentation of treatment status of the member (treatment-naïve or treatment-experienced);
5. Documentation of cirrhosis status of the member (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
6. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
7. Age ≥ 12 years or body weight ≥ 35kg;

8. If age ≥ 18 years, member has at least one of the following contraindications to Mavyret (a or b):
   a. Decompensated cirrhosis (Child-Pugh B or C) confirmed by lab findings and clinical notes;
   b. Receiving treatment with efavirenz or atazanavir;
   **See Appendix E for additional details on acceptable contraindications*
9. If age ≥ 18 years and contraindicated to Mavyret, member must use Epclusa®, unless contraindicated or clinically significant adverse effects are experienced;
10. Life expectancy ≥ 12 months with HCV treatment;
11. Documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy, if applicable;
12. Member agrees to participate in a medication adherence program including 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;
13. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V for reference*);
14. Dose does not exceed ledipasvir 90 mg and sofosbuvir 400 mg per day (1 tablet/day).

**Approval duration: up to a total of 24 weeks***
*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

**B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

## II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Must meet both of the following (i and ii):
      i. Documentation supports that member is currently receiving Harvoni for chronic HCV infection and has recently completed at least 60 days of treatment with Harvoni;
      ii. Confirmed HCV genotype is 1, 4, 5, or 6;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed ledipasvir 90 mg and sofosbuvir 400 mg per day (1 tablet/day).

**Approval duration: up to a total of 24 weeks***
*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

**A. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – HIM.PHAR.21 for health insurance marketplace or evidence of coverage documents.

**IV. Appendices/General Information**

*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
IDSA: Infectious Diseases Society of America
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
RBV: ribavirin
RNA: ribonucleic acid

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Mavyret™ (glecaprevir /pibrentasvir) | Treatment-naïve Chronic hepatitis C (CHC) infection:<br>**Genotypes 1, 4, 5, or 6**<br><br>Without cirrhosis:<br>3 tablets PO QD for 8 weeks<br><br>With compensated cirrhosis:<br>3 tablets PO QD for 12 weeks | Mavyret:<br>glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day |
| Mavyret™ (glecaprevir /pibrentasvir) | Treatment-experienced with IFN/pegIFN + RBV +/- sofosbuvir CHC infection:<br>**Genotypes 1, 4, 5, or 6**<br><br>Without cirrhosis:<br>3 tablets PO QD for 8 weeks<br><br>With compensated cirrhosis:<br>3 tablets PO QD for 12 weeks | Mavyret:<br>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:<br>**Genotype 1**<br><br>Without cirrhosis or with compensated cirrhosis:<br>3 tablets PO QD for 16 weeks | Mavyret:<br>glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Mavyret™ (glecaprevir /pibrentasvir) | Treatment-experienced with NS3/4A protease inhibitor without prior NS5A inhibitor CHC infection:<br>**Genotype 1**<br><br>Without cirrhosis or with compensated cirrhosis:<br>3 tablets PO QD for 12 weeks | Mavyret:<br>glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day |
| Epclusa® (sofosbuvir/ velpatasvir) | Without cirrhosis or with compensated cirrhosis, treatment-naïve or treatment-experienced:<br>**Genotypes 1, 4, 5, or 6**<br><br>One tablet PO QD for 12 weeks | Epclusa:<br>sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) 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*

- If used in combination with RBV, all contraindications to RBV also apply to Harvoni combination therapy.

*Appendix D: Direct-Acting Antivirals for Treatment of HCV Infection*

| Brand Name | Drug Class | | | | |
|---|---|---|---|---|---|
| | NS5A Inhibitor | Nucleotide Analog NS5B Polymerase Inhibitor | Non-Nucleoside NS5B Palm Polymerase Inhibitor | NS3/4A Protease Inhibitor (PI) | CYP3A Inhibitor |
| Daklinza | Daclatasvir | | | | |
| Epclusa* | Velpatasvir | Sofosbuvir | | | |
| Harvoni* | Ledipasvir | Sofosbuvir | | | |
| Mavyret* | Pibrentasvir | | | Glecaprevir | |
| Olysio | | | | Simeprevir | |
| Sovaldi | | Sofosbuvir | | | |
| Technivie* | Ombitasvir | | | Paritaprevir | Ritonavir |
| Viekira XR/PAK* | Ombitasvir | | Dasabuvir | Paritaprevir | Ritonavir |
| Vosevi* | Velpatasvir | Sofosbuvir | | Voxilaprevir | |
| Zepatier* | Elbasvir | | | Grazoprevir | |

*Combination drugs

*Appendix E: 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.

- Treatment with Harvoni for 8 weeks can be considered in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL. In the ION-3 trial, patients with a baseline HCV viral load of < 6 million IU/mL and were treated with Harvoni for 8 weeks achieved SVR-12 at a rate of 97% versus 96% of those treated with Harvoni for 12 weeks.
- Acceptable medical justification for inability to use Mavyret (preferred product):
  - Severe hepatic disease (Child-Pugh C): use of Mavyret is not recommended due to higher exposures of glecaprevir and pibrentasvir.
    - Alternatives on the formulary: Harvoni, Epclusa, Sovaldi, Daklinza
  - Moderate hepatic disease (Child-Pugh B): although not an absolute contraindication, use of Mavyret is not recommended in patients with moderate hepatic disease (Child-Pugh B) due to lack of safety and efficacy data.
    - Alternatives on the formulary: Harvoni, Epclusa, Sovaldi, Daklinza
    - Following administration of Mavyret in HCV infected subjects with *compensated* cirrhosis (Child-Pugh A), exposure of glecaprevir was approximately 2-fold and pibrentasvir exposure was similar to non-cirrhotic *HCV infected* subjects.
    - At the clinical dose, compared to *non-HCV infected* subjects with *normal hepatic function*, glecaprevir AUC was 100% higher in Child-Pugh B subjects, and increased to 11-fold in Child-Pugh C subjects. Pibrentasvir AUC was 26% higher in Child-Pugh B subjects, and 114% higher in Child-Pugh C subjects.
  - Drug-drug interactions with one or more the following agents:
    - Atazanavir
      - Alternatives on the formulary: Harvoni, Epclusa, Sovaldi, Daklinza
    - Efavirenz:
      - Alternatives on the formulary: Harvoni, Sovaldi, Daklinza
- Child-Pugh Score

| | 1 Point | 2 Points | 3 Points |
|---|---|---|---|
| Bilirubin | Less than 2 mg/dL<br>Less than 34 umol/L | 2-3 mg/dL<br>34-50 umol/L | Over 3 mg/dL<br>Over 50 umol/L |
| Albumin | Over 3.5 g/dL<br>Over 35 g/L | 2.8-3.5 g/dL<br>28-35 g/L | Less than 2.8 g/dL<br>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<br>Grade I-II | Moderate-severe / poorly controlled.<br>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

- Unacceptable medical justification for inability to use Mavyret (preferred product):
  - Black Box Warning (BBW): currently or previously infected with hepatitis B virus. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class

of direct-acting antivirals for treatment of HCV infection. Therefore it is not a valid clinical reason not to use Mavyret.

- Concurrent anticoagulant therapy: Fluctuations in International Normalized Ratio (INR) have been observed in warfarin recipients who were also receiving treatment for HCV infections. This BBW is not unique to Mavyret, and it applies across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection. Although caution is advised when using Mavyret while receiving concurrent anticoagulant therapy, specifically warfarin, this is not an absolute contraindication as long as patient is adequately monitored and educated during therapy.
- Drug-drug interactions with one or more of the following agents:
  - Rifampin, carbamazepine, or St. John's wort:
    - Alternatives on the formulary: none
    - These drug-drug interactions are not unique to Mavyret, and they apply across the entire therapeutic class of direct-acting antivirals for treatment of HCV infection.

- The World Health Organization (WHO) estimates that at the global level, there are approximately 2,278,400 HIV-HCV co-infections (IQR 1,271,300 to 4,417,000) of which 1,362,700 (IQR 847,770 to 1,381,800) in people who inject drugs (PWID), equaling an overall co-infection prevalence in HIV-infected individuals of **6.2%** (IQR 3.4 to 1.9). In North America specifically, the meta-analysis showed that the best estimate for the percentage of total HIV-infected individuals with HCV co-infection was about **14%.** On the other hand, the Centers of Disease Control and Prevention (CDC) estimates that about **25%** of people with HIV in the US are co-infected with HCV.
  - As of March 2018, there are a total of 1.38 million members enrolled in Centene Health Insurance Marketplace. Out of those members, about 6,300 members are estimated to be diagnosed with HIV based on claims data, with about 173 members with recent claims for atazanavir and/or efavirenz. And based on the CDC as well as WHO prevalence estimation for North America, we can predict that about 14% to 25%, or 882 to 1,575 members, with HIV infection may be co-infected with HCV, with about 25 to 44 members who may not be eligible for treatment with Mavyret due to drug interactions involving atazanvir and/or efavirenz.

## V. Dosage and Administration

| **Indication: Adult patients with chronic HCV infection** | | | |
|---|---|---|---|
| **Indication** | **Dosing Regimen** | **Maximum Dose** | **Reference** |
| Genotype 1 chronic HCV infection: | One tablet PO QD for:<br><br>Treatment-naïve adult patients without cirrhosis AND whose HCV viral load is less than 6 million IU/mL: for 8 weeks (12 weeks for black and/or HIV-coinfected patients)ǂ<br><br>Treatment-naïve adult patients with compensated cirrhosis: for 12 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated September 2017) |

| Indication: Adult patients with chronic HCV infection | | | |
|---|---|---|---|
| **Indication** | **Dosing Regimen** | **Maximum Dose** | **Reference** |
| | Treatment-experienced with pegIFN/ RBV adult patients without cirrhosis: for 12 weeks<br><br>Treatment-experienced with pegIFN/ RBV adult patients with compensated cirrhosis: Harvoni plus weight-based RBV‡ for 12 weeks<br><br>Treatment-experienced with NS3 PI*/pegIFN/RBV adult patient without cirrhosis for 12 weeks<br><br>Treatment-experienced with NS3 PI*+/- pegIFN/RBV adult patients with compensated cirrhosis: Harvoni plus weight-based RBV for 12 weeks<br><br>Treatment-experienced with Sofosbuvir (but not with simeprevir) without cirrhosis: Harvoni plus weight-based RBV for 12 weeks | | |
| Genotype 1, 4‡, 5‡, or 6‡ with decompensated cirrhosis:<br>Adult patients who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma | One tablet PO QD plus low initial dose of RBV (600 mg, increased as tolerated) for 12 weeks Or without RBV for 24 weeks if RBV ineligible | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated September 2017) |
| Genotype 1, 4, 5, or 6 with decompensated cirrhosis:<br>Adult patients in whom a previous sofosbuvir-containing regimen has failed‡ | One tablet PO QD with low initial dose of RBV (600 mg, increased as tolerated) for 24 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | AASLD-IDSA (updated September 2017) |
| Genotype 1 or 4 post-liver transplantation:<br>Treatment-naive and treatment-experienced adult patients without | One tablet PO QD plus RBV for 12 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated |

| Indication: Adult patients with chronic HCV infection | | | |
|---|---|---|---|
| **Indication** | **Dosing Regimen** | **Maximum Dose** | **Reference** |
| cirrhosis, with compensated cirrhosis, or with decompensated cirrhosis | | | September 2017) |
| Genotype 4, 5, or 6: Treatment-naive adult patients with or without compensated cirrhosis | One tablet PO QD for 12 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated September 2017) |
| Genotype 4: Treatment-experienced** adult patients without compensated cirrhosis | One tablet PO QD for 12 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated September 2017) |
| Genotype 4:<br><br>Treatment-experienced** adult patients with compensated cirrhosis | One tablet PO QD plus weight-based RBV for 12 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated September 2017) |
| Genotype 5 or 6: Treatment-experienced** adult patients with or without compensated cirrhosis | One tablet PO QD for 12 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | 1) FDA-approved labeling<br>2) AASLD-IDSA (updated September 2017) |

*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.*
** NS3 protease inhibitor = telaprevir, boceprevir, or Simeprevir*
*Treatment-experienced refers to previous treatment with peginterferon/RBV unless otherwise stated*
*ǂ Off-label, AASLD-IDSA guideline-supported dosing regimen*

| Indication: Pediatric patients (age ≥ 12 years or weighing at least 35 kg) with chronic HCV infection | | | |
|---|---|---|---|
| **Indication** | **Dosing Regimen** | **Maximum Dose** | **Reference** |
| Genotype 1 chronic HCV infection | One tablet PO QD for: | One tablet (sofosbuvir 400 | FDA-approved labeling |

| Indication: Pediatric patients (age ≥ 12 years or weighing at least 35 kg) with chronic HCV infection | | | |
|---|---|---|---|
| **Indication** | **Dosing Regimen** | **Maximum Dose** | **Reference** |
| | Treatment naïve pediatric patients (≥12 years of >35 kg) without cirrhosis or with compensated cirrhosis regardless of baseline viral load: for 12 weeks<br><br>Treatment-experienced with pegIFN/RBV pediatric (≥12 years of ≥35 kg) without cirrhosis: for 12 weeks<br><br>Treatment-experienced pediatric patients (≥12 years of >35 kg) with compensated cirrhosis: for 24 weeks | mg / ledipasvir 90 mg) per day | |
| Genotype 4, 5, or 6 chronic HCV infection | Treatment-naive or treatment-experienced pediatric (≥12 years of ≥35 kg) patients with or without compensated cirrhosis:<br><br>One tablet PO QD for 12 weeks | One tablet (sofosbuvir 400 mg / ledipasvir 90 mg) per day | FDA-approved labeling |

## VI. Product Availability

Tablet: 400 mg sofosbuvir with 90 mg ledipasvir

## VII. References

1. Harvoni Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; November 2017. Available at http://www.harvoni.com. Accessed May 1, 2018.
2. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). HCV guidance: recommendations for testing, managing, and treating hepatitis C. Last updated September 21, 2017. Available at: https://www.hcvguidelines.org/. Accessed May 1, 2018.
3. Wirth S, Gonzalez-Peralta R, Rosenthal P, et al. Sofosbuvir-Containing Regimens are Safe and Effective in Adolescents with Chronic hepatitis C Infection. The 26th Annual Meeting of the Asian pacific Association for the Study of the Liver (APASL) in February 15-19, 2017 in Shanghai, China.
4. Squires JE, Balisteri WF. Hepatitis C Virus Infection in Children and Adolescents. Hepatology Communications 2017; 1(2): 87-98.
5. Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. Lanet Infect Dis 2016;16:797-808. http://dx.doi.org/10.1016/
6. Centers for Disease Control and Prevention. HIV and viral hepatitis: fact sheet. June 2016. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf. Accessed March 13, 2018.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| New policy created.<br>In relation to the current CP.PHAR.17 Hepatitis C Therapies policy, please note the following modifications or additions:<br>• HCV RNA levels over six-month period added to confirm infection is chronic per AASLD guidelines.<br>• Life expectancy "greater than or equal to 12 months if HCC and awaiting transplant" is modified to indicate "greater than or equal to 12 months with HCV therapy" per AASLD guidelines.<br>• Testing criteria reorganized by "no cirrhosis"/"cirrhosis" consistent with the regimen tables; HCC population is included under "cirrhosis" and broadened to incorporate HCC amenable to curative measures (resection, ablation, transplant) per the AASLD HCC guidelines (guidelines are added to the reference section). In the regimen tables, HCC can fall under compensated or decompensated cirrhosis but not under "no cirrhosis" per section I criteria.<br>• Methods to diagnose fibrosis/cirrhosis are modified to require presence of HCC, liver biopsy or a combination of one serologic and one radiologic test per AASLD guidelines. Serologic and radiologic tests are updated and correlated with METAVIR per Appendix B. Note that Hepascore has been discontinued and that both LabCorp and Quest offer FibroTest. FibroSpect II has been recently updated to correlate with METAVIR F3/F4 and is offered now by Prometheus rather than Quest. APRI and FIB-4 are calculations based on AST and platelets.<br>• Removed creatinine clearance restriction – not a contraindication.<br>• Criteria added excluding post-liver transplantation unless regimens specifically designate.<br>• Dosing regimens are presented in Appendix D and E per AASLD guidelines and FDA-approved indications.<br>• The initial approval period is shortened to 8 weeks to accommodate verification of HCV RNA status within that time - AASLD guidelines recommended testing at 4 and 6 weeks. | 08.16 | 08.16 |
| Added pediatric (≥12 years or ≥35 kg) indication expansion for genotype 1,4,5,6. Updated contraindications.<br>Allowed full therapy regimen at initial approval duration. | 04.17 | 08.17 |
| Added preferencing requiring Mavyret for FDA-approved indications. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Exception made to require Hep B screening for all patients prior to treatment to ensure that proper risk reduction measures are taking, though this is not specifically addressed in boxed warning. | 08.17 | |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 3Q18 annual review; added baseline viral load requirement for treatment-naïve adult with GT 1 for determination of treatment duration; added specific scenarios of clinically acceptable and unacceptable rationale for inability to use Mavyret; removed requirement for contraindications such as pregnancy and CrCl with RBV; expanded duration of tx required for COC from 30 days to 60 days; required verification of genotype for COC; removed requirement for advanced liver disease; references reviewed and updated. | 05.22.18 | 06.18 |
| No significant changes :added financial redirection to Epclusa for those unable to use Mavyret. | 07.05.18 | |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise

professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**
**For Health Insurance Marketplace members,** when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.