Clinical Policy: sofosbuvir/velpatasvir (Epclusa)
Reference Number: NM.CP.PPA.03
Effective Date: 1/1/19
Last Review Date: 1/11/23
Revision Log

Description and FDA Approved Indication(s)
Sofosbuvir/velpatasvir (Epclusa®) is a fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor. Epclusa is indicated for the treatment of adult and pediatric patients 3 years of age and older with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection:

- Without cirrhosis or with compensated cirrhosis
- With decompensated cirrhosis for use in combination with ribavirin (RBV)

Black Box Warning
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 who were not receiving HBV antiviral therapy, leading to fulminant hepatitis, hepatic failure, and death, in some cases. Cases have been reported in patients who are HBsAg positive and also in patients with serologic evidence of resolved HBV infection (i.e., HBsAg negative and anti-HBc positive). HBV reactivation has also been reported in patients receiving certain immunosuppressant or chemotherapeutic agents; the risk of HBV reactivation associated with treatment with HCV direct-acting antivirals may be increased in these patients. In patients with serologic evidence of current or prior HBV infection, monitor for HBV reactivation and hepatitis flare during HCV treatment and post-treatment follow-up, with treatment of HBV infection as clinically indicated.

Product Availability
Oral tablet
Generic: sofosbuvir/velpatasvir 400 mg/100 mg
Brand: (Epclusa) sofosbuvir/velpatasvir 400 mg/100 mg, 200mg/50mg
Oral pellets in unit-dose packets
Brand: (Epclusa) sofosbuvir/velpatasvir 150 mg/37.5 mg, 200mg/50mg

Policy/Criteria

It is the policy of Western Sky Community Care (WSCC) that **Epclusa** is **medically necessary** when the following criteria are met:

1. **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. Documentation of the treatment status of the patient (treatment-naive or treatment-experienced);

3. Documentation of cirrhosis status of the patient (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
4. Age ≥ 3 years;
5. Life expectancy ≥ 12 months with HCV treatment (this can be assumed unless lower life expectancy explicitly stated in chart notes or member diagnosed with hepatocellular carcinoma);
6. ****Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see appendices C & D)*;
7. ****Dose as follows (a or b): For pediatric patients age at least 3 years old:
    a. For pediatric patients age at least 3 years old:
        i. If weighs less than 17 kg: one 150mg/37.5 mg packet of pellets once daily **(only available as BRAND)**
        ii. If weighs 17 kg to less than 30 kg: one 200mg/50mg packet of pellets or tablet once daily **(only available as BRAND)**
        iii. If weighs 30 kg or more: one 400mg/100mg tablet daily ***(approve only generic tab)***
    b. For adults: one 400 mg/100 mg tablet daily ***(approve only generic tab)***
8. Member has no contraindications to sofosbuvir/velpatasvir and ribavirin (if ribavirin is being prescribed):
    a. Epclusa and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated. Refer to the ribavirin prescribing information for a list of contraindications for ribavirin.

Approval duration: up to a total of 24 weeks (if adult is ribavirin ineligible), only approve brand if dose requires only 1 tablet or oral pellet packet of 150mg/37.5 mg or 200mg/50mg per day, otherwise approve generic tab. *(Approved duration should be consistent with AASLD guidelines--see appendices C and D)*

****If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen is determined after consultation with Project ECHO—please approve regimen.**

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): CP.PMN.53 for Medicaid.
2. If denial is likely please reach out to prescriber's office for peer-to-peer.

2. Continued Therapy

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

1. Member meets one of the following (a or b):

a. Currently receiving medication or member has previously met initial approval criteria;
b. Documentation supports that member is currently receiving Epclusa or generic Epclusa for chronic HCV infection;

2. Member is responding positively to therapy;
3. ****Dose as follows (a or b):
    a. For pediatric patients age at least 3 years old:
        i. If weighs less than 17 kg: one 150mg/37.5 mg packet of pellets once daily **(only available as BRAND)**
        ii. If weighs 17 kg to less than 30 kg: one 200mg/50mg packet of pellets or tablet once daily **(only available as BRAND)**
        iii. If weighs 30 kg or more: one 400mg/100mg tablet daily ***(approve only generic tab)***
    b. For adults: one 400 mg/100 mg tablet daily ***(approve only generic tab)***

Approval duration: As needed for completion of 12-24 weeks (24 week completion only if adult is ribavirin ineligible), only approve brand if dose requires only 1 tablet or oral pellet packet of 150mg/37.5 mg or 200mg/50mg per day, otherwise approve generic tab. *(Approved duration should be consistent with guidelines--see appendices C and D)*

******If treatment regimen varies in dosing or interval from FDA or AASLD-IDSA guideline recommendations but it is documented on PA request/office chart notes that requested regimen is determined after consultation with Project ECHO—please approve regimen.**

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): CP.PMN.53 for Medicaid.

2. 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 policies –CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Treatment-experienced patients with both NS3/4A PI AND NS5A inhibitor, such as combination therapies including: Technivie, Viekira, and Zepatier.

Appendices

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
APRI: AST to platelet ratio
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
HIV: human immunodeficiency virus

IDSA: Infectious Diseases Society of America
IQR: interquartile range
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
PegIFN: pegylated interferon
PI: protease inhibitor
RBV: ribavirin
RNA: ribonucleic acid

***Serologic tests:**
FibroTest (available through Quest as FibroTest or LabCorp as FibroSure)
FIBROSpect II (available through Prometheus Laboratory)
APRI (AST to platelet ratio index)
FIB-4 (Fibrosis-4 index: includes age, AST level, platelet count)

†Radiologic tests:
FibroScan (transient elastography)
MRE (magnetic resonance elastography)

‡Liver biopsy (histologic scoring systems):
METAVIR F3/F4 is equivalent to Knodell, Scheuer, and Batts-Ludwig F3/F4 and Ishak F4-5/F5-6
METAVIR fibrosis stages: F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = few septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis

Appendix B: 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***Additional PIs no longer recommended that have been discontinued: Victrelis (boceprevir), Incivek (telaprevir)*

Appendix C: Epclusa treatment duration

Genotype	Patient Population	Regimen and Duration
1, 2, 3, 4, 5, 6	Treatment-naïve and treatment-experienced[a], without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa 12 weeks
	Treatment-naïve and treatment-experienced[a], with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + ribavirin 12 weeks

a. In clinical trials, regimens contained peginterferon alfa/ribavirin with or without an HCV NS3/4A PI (boceprevir, simeprevir, or telaprevir).

Appendix D: AASLD-IDSA Recommended Regimens and Treatment Durations
https://www.hcvguidelines.org/

Appendix E:
Any of the following meet the definition for cirrhosis per NM state directives:

- APRI >= 1.0
- Fib-4 >= 3.25
- Transient Elastography Score >= 12.5 dP3 (F4 equivalent)
- Fibrotest >= 0.73 (f4 equivalent) OR Fibrometer with F4 predominance
- Radiographic imaging or physical exam findings consistent with cirrhosis
- Liver biopsy confirming a METAVIR score of F4

Child-Pugh Score:

	1 Point	2 Points	3 Points
Bilirubin	Less than 2 mg/dL Less than 34 umol/L	2-3 mg/dL 34-50 umol/L	Over 3 mg/dL Over 50 umol/L
Albumin	Over 3.5 g/dL Over 35 g/L	2.8-3.5 g/dL 28-35 g/L	Less than 2.8 g/dL Less than 28 g/L
INR	Less than 1.7	1.7 - 2.2	Over 2.2
Ascites	None	Mild / medically controlled (diuretic responsive)	Moderate-severe / poorly controlled (diuretic refractory)
Encephalopathy	None	Mild / medically controlled Grade I-II	Moderate-severe / poorly controlled. 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

Appendix F: Contraindications

- 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.

References

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Revision Log

Reviews, Revisions, and Approvals	Date	Approval Date
New clinical policy created for WSCC based on New Mexico requirements	11/18	11/18
Added provision for approval of drug dosing and interval (despite not meeting AASLD and IDSA recommended guidelines) if regimen is recommended/requested after consultation with Project ECHO; added Project ECHO to references; JJM	1/25/19	1/25/19
Renamed clinical policy per corporate guidelines; Changed from NM.CP.PHAR.03 to NM.CP.PPA.03; Name presented at WSCC P&T Committee	3/20/19	3/20/19
Edited required materials that provider must submit to include various PA forms AND Uniform NM HCV Checklist; Removed need for contraindication to Mavyret; removed section in Appendix F which lists acceptable medical justification for inability to use Mavyret. Removed instruction to edit co-pay to $0. Removed “If denial is likely please make attempt to prescriber’s office for peer-to-peer”	9/9/19	
Edited dosage forms section.	10/16/19	
Edited Appendix C: Epclusa duration of treatment table. Reviewed and approved by WSCC P&T Committee.		10/23/19
Annual Review. References updated. Reviewed and approved by WSCC P&T Committee.		1/29/20
Added additional direction for life expectancy > 12 months to be assumed unless explicitly stated in chart notes or member has diagnosis of hepatocellular carcinoma.	6/26/20	
Reviewed and approved by WSCC P&T Committee.		7/8/20
Edited criteria to match updated directive from NM HSD, MAD Supplement 20-13 to include updated forms. Updated references to reflect this change in NM Medicaid direction.	1/12/21	
Annual review. Removed requirement for genotype. Added pediatric dosing and indications. Edited age limit and dosing requirements. Reviewed and approved by WSCC P&T Committee.		1/20/21
Updated product availability. Updated age limit based on FDA approval for pediatric patients more than or equal to 3	10/26/21	

Reviews, Revisions, and Approvals	Date	Approval Date
years of age. Updated approvable dosing limits based on age and weight for pediatric patients. Edited references and links to NM HCV Uniform HCV checklist.		
Reviewed and approved by WSCC P&T Committee.		11/3/21
Annual review. Reviewed and approved by WSCC P&T Committee.		1/12/22
Updated dosing portion from “Dose does not exceed” to “Dose as follows” to prevent underdosing for pediatric members.	10/10/22	
Updated wording on dosage. Reviewed and approved by WSCC P&T Committee.		10/12/22
Annual Review. Updated References. Removed requirement for Drug Authorization Form and Uniform New Mexico HCV Checklist. Reviewed and approved by WSCC P&T Committee.	1/9/23	1/11/23