Clinical Policy: Daclatasvir (Daklinza)

Reference Number: CP. PCH.15
Effective Date: 01.01.20
Last Review Date: 02.20
Line of Business: Commercial, HIM

Revision Log

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

Description

Daclatasvir (Daklinza™) is a hepatitis C virus (HCV) NS5A inhibitor.

FDA Approved Indication(s)

Daklinza is indicated for use with sofosbuvir, with or without ribavirin, for the treatment of chronic HCV genotype 1 or 3 infection.

Limitation(s) of use: Sustained virologic response (SVR12) rates are reduced in genotype 3 patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

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 Daklinza 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, 2, 3, 4, 5, or 6;
   **Chart note documentation and copies of lab results are required*
3. Documentation of the treatment status of the patient (treatment-naive or treatment-experienced);
4. Documentation of cirrhosis status of the patient (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
5. Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease physician, or provider who has expertise in treating HCV based on a certified training program (*see Appendix F*);
6. Age ≥ 18 years;
7. Prescribed for use in combination with Sovaldi®;
8. For genotype 1a with cirrhosis, laboratory testing confirming the absence of NS5A resistance-associated polymorphisms at amino acid positions M28, Q30, L31 and Y93;
9. Member must meet one of the following (a, b, or c):
   a. For adults with genotype 1: Member must use Harvoni® (*authorized generic or brand for 8 weeks only*), sofosbuvir/velpatasvir (Epclusa®) (*authorized generic*

preferred), Mavyret™, or Zepatier® unless all are contraindicated or clinically significant adverse effects are experienced;
   b. For adults with genotype 4: Member must use sofosbuvir/velpatasvir (Epclusa) (*authorized generic preferred*), Mavyret, or Zepatier unless all are contraindicated or clinically significant adverse effects are experienced;
   c. For adults with genotype 2, 3, 5, or 6: Member must use sofosbuvir/velpatasvir (Epclusa) (*authorized generic preferred*) or Mavyret, unless all are contraindicated or clinically significant adverse effects are experienced;
10. Life expectancy ≥ 12 months with HCV treatment;
11. Member agrees to participate in a medication adherence program meeting 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;
12. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
13. Dose does not exceed 90 mg (1 tablet) per 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): CP.CPA.09 for commercial and 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. Documentation supports that member is currently receiving Daklinza for chronic HCV infection and has recently completed at least 60 days of treatment with Daklinza;
2. Member is responding positively to therapy;
3. Dose does not exceed 90 mg (1 tablet) per 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): CP.CPA.09 for commercial and 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 policies – CP.CPA.09 for commercial and 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
Harvoni® (sofosbuvir/ ledipasvir)	Without cirrhosis, treatment-naïve, whose HCV viral load is less than 6 million IU/mL: **Genotypes 1** One tablet PO QD for 8 weeks	Harvoni: sofosbuvir 400 mg/ ledipasvir 90 mg (1 tablet) per day
Epclusa® (sofosbuvir/ velpatasvir)	Without cirrhosis or with compensated cirrhosis, treatment naïve or treatment experienced: **Genotypes 1 through 6** One tablet PO QD for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Epclusa® (sofosbuvir/ velpatasvir) plus RBV	With decompensated cirrhosis (Child-Pugh class B or C) treatment-naïve or treatment experienced: **Genotypes 1 through 6** One tablet PO QD plus weight-based RBV for 12 weeks	Epclusa: sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Mavyret™ (glecaprevir/ pibrentasvir	Treatment-naïve: **Genotypes 1, 2, or 3** Without cirrhosis or with compensated cirrhosis: Three tablets PO QD for 8 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Mavyret™ (glecaprevir/ pibrentasvir	Treatment-experienced with IFN/pegIFN + RBV: **Genotypes 1, 2, or 3** Without cirrhosis: Three tablets PO QD for 8 weeks **Genotype 3** With compensated cirrhosis: Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Mavyret™ (glecaprevir/ pibrentasvir	Treatment-naïve or treatment-experienced, post-liver transplantation in the allograft with or without compensated cirrhosis: **Genotypes 1, 4, 5, or 6** Three tablets PO QD for 12 weeks	Mavyret: glecaprevir 300 mg/ pibrentasvir 120 mg (3 tablets) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a:** Treatment-naïve or pegIFN/RBV-experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a:** Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1b:** Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis One tablet PO QD for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a or 1b:** pegIFN/RBV/NS3 PI*‡ -experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Zepatier® (grazoprevir/ elbasvir)	**Genotype 1a or 1b:** pegIFN/RBV/NS3 PI*‡ -experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93 One tablet PO QD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 3‡:** pegIFN/RBV-experienced with compensated cirrhosis One tablet PO QD plus sofosbuvir 400 mg for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 4:** Treatment-naïve with or without compensated cirrhosis One tablet PO QD for 12 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) per day
Zepatier® (grazoprevir/ elbasvir)	**Genotype 4:** PegIFN/RBV-experienced with or without compensated cirrhosis with virologic relapse/failure Virologic relapse after prior pegIFN/RBV therapy: One tablet PO QD for 12 weeks Virologic failure while on pegIFN/RBV therapy: One tablet PO QD plus weight-based RBV for 16 weeks	One tablet (grazoprevir 100 mg/ elbasvir 50 mg) 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/Boxed Warnings

- Contraindication(s):
  - When Daklinza is used in combination with other agents, the contraindications applicable to those agents are applicable to the combination regimen. Refer to the respective prescribing information for a list of contraindications.
  - Daklinza is contraindicated in combination with drugs that strongly induce CYP3A and, thus, may lead to lower exposure and loss of efficacy of Daklinza. Contraindicated drugs include, but are not limited to: phenytoin, carbamazepine, rifampin, and St. John's wort.
- Boxed warning(s): risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV

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	

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)	CYP3A Inhibitor
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.
- For patients infected with HCV Genotype 1a with cirrhosis: Testing for the presence of virus with NS5A resistance-associated polymorphisms is recommended.
- According to the September 2017 AASLD/IDSA HCV guidance updates, Daklinza plus Sovaldi is a treatment option for patients with genotypes 1 through 6 in decompensated cirrhosis and post-liver transplantation in the allograft.
- 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

	1 Point	2 Points	3 Points
Ascites	None	Mild / medically controlled	Moderate-severe / poorly controlled
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: Healthcare Provider HCV Training
Acceptable HCV training programs and/or online courses include, but are not limited to the following:

- Hepatitis C online course (https://www.hepatitisc.uw.edu/): University of Washington is funded by the Division of Viral Hepatitis to develop a comprehensive, online self-study course for medical providers on diagnosis, monitoring, and management of hepatitis C virus infection. Free CME and CNE credit available.
- Fundamentals of Liver Disease (https://liverlearning.aasld.org/fundamentals-of-liver-disease): The AASLD, in collaboration with ECHO, the American College of Physicians (ACP), CDC, and the Department of Veterans Affairs, has developed Fundamentals of Liver Disease, a free, online CME course to improve providers' knowledge and clinical skills in hepatology.
- Clinical Care Options: http://www.clinicaloptions.com/hepatitis.aspx
- CDC training resources: https://www.cdc.gov/hepatitis/resources/professionals/trainingresources.htm

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1: Treatment-naïve or treatment-experienced without cirrhosis	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD for 12 weeks	Daklinza: 90 mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Genotype 1, 2‡, 3 or 4‡: Decompensated cirrhosis (including those with hepatocellular carcinoma)	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD with low initial dose of RBV (600 mg) and increased as tolerated for 12 weeks	Daklinza: 90 mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Genotype 1, 2‡, 3, or 4‡: Decompensated cirrhosis (including those with hepatocellular carcinoma) and intolerant to RBV	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD for 24 weeks	Daklinza: 90 mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Genotype 1, 4‡, 5‡, or 6‡: Treatment-naïve or	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO	Daklinza: 90 mg per day	1) FDA-approved

Indication	Dosing Regimen	Maximum Dose	Reference
treatment-experienced, post-liver transplantation in the allograft with or without compensated cirrhosis	QD with low initial dose of RBV (600 mg) and increased as tolerated for 12 weeks		labeling 2) AASLD-IDSA (updated May 2018)
Genotype 2ǂ: Treatment- naïve or treatment- experienced without cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 12 weeks	Daklinza: 90 mg per day	AASLD-IDSA (updated May 2018)
Genotype 2ǂ: Treatment-naïve or treatment-experienced with compensated cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 16 to 24 weeks	Daklinza: 90 mg per day	AASLD-IDSA (updated May 2018)
Genotype 2ǂ or 3: Treatment-naïve or treatment-experienced, post-liver transplantation in the allograft with or without compensated or decompensated cirrhosis	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD with low initial dose of RBV (600 mg) and increased as tolerated for 12 weeks	Daklinza: 90 mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Genotype 3: Treatment- naïve or treatment-experienced without cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 12 weeks	Daklinza: 90 mg per day	1) FDA-approved labeling 2) AASLD-IDSA (updated May 2018)
Genotype 3: Treatment- naïve with compensated cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD with or without weight-based RBV for 24 weeks	Daklinza: 90 mg per day	AASLD-IDSA (updated May 2018
Daklinza dose modification	Reduce dosage to 30 mg PO QD with strong CYP3A4 inhibitors and increase to 90 mg PO QD with moderate CYP3A inducers.	Daklinza: 90 mg per day	FDA-approved labeling

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.
Treatment-experienced refers to previous treatment with peginterferon/RBV unless otherwise stated ǂ Off-label, AASLD-IDSA guideline-supported dosing regimen

VI. Product Availability

Tablets: 30 mg, 60 mg, 90 mg

VII. References

1. Daklinza Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; November 2017. Available at: http://packageinserts.bms.com/pi/pi_daklinza.pdf. Accessed April 30, 2019.
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 May 24, 2018. Available at: https://www.hcvguidelines.org/. Accessed April 30, 2019.
3. Wolitski R. When it comes to curing hepatitis c, your health care provider may not need to be a specialist. U.S. Department of Health & Human Services. Last updated September 20, 2017. Available at: https://www.hhs.gov/hepatitis/blog/2017/09/20/study-calls-for-expansion-of-hepatitis-c-treatment.html. Accessed October 30, 2019.
4. CDC. Viral hepatitis: Q&As for health professionals. Last updated July 2, 2019. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed October 30, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created; per SDC and prior clinical guidance added HIM line of business to the existing Commercial policy (modified policy number to CP.PCH.15, retired HIM.PA.SP27 and CP.CPA.283); added requirement that life expectancy ≥ 12 months with HCV treatment and participation in a medication adherence program.	12.03.19	02.20
Added new prescriber requirement to include a "provider who has expertise in treating HCV based on a certified training program"; Appendix F (Healthcare Provider HCV Training) added; updated Mavyret dosing recommendations to 8 weeks total duration of therapy for treatment-naïve HCV with compensated cirrhosis across all genotypes (1-6).	11.07.19	02.20

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.

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