Clinical Policy: Daclatasvir (Daklinza)

Reference Number: HIM.PA.SP27
Effective Date: 01.01.17
Last Review Date: 08.20
Line of Business: 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.

* *This criteria does NOT apply to California Commercial Exchange Plans.*

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 or 3;
   **Chart note documentation and copies of lab results are required*
3. Documentation of treatment status of the member (treatment-naïve or treatment-experienced);
4. Documentation of cirrhosis status of the member (no cirrhosis, compensated cirrhosis, or decompensated cirrhosis);
5. Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease specialist, 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 use Epclusa® or Vosevi®, unless clinically significant adverse effects are experienced or all are contraindicated
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 12 weeks

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. 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 12 weeks

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.

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
sofosbuvir/velpatasvir (Epclusa®)	**Genotypes 1 through 6** Without cirrhosis or with compensated cirrhosis, treatment naïve or pegIFN/ RBV-experienced: One tablet PO QD for 12 weeks	sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
sofosbuvir/velpatasvir (Epclusa®)	**Genotypes 1 through 6** With decompensated cirrhosis treatment-naïve or treatment experienced: One tablet PO QD plus weight-based RBV for 12 weeks	sofosbuvir 400 mg/ velpatasvir 100 mg (1 tablet) per day
Vosevi® (sofosbuvir/ velpatasvir/ voxilaprevir)	**Genotype 1-6** treatment-experienced with NS5A inhibitor* with or without compensated cirrhosis: One tablet PO QD for 12 weeks	One tablet (sofosbuvir 400 mg/ velpatasvir 100 mg/ voxilaprevir 100 mg) per day
Vosevi® (sofosbuvir/ velpatasvir/ voxilaprevir)	**Genotype 1a or 3** treatment-experienced with a sofosbuvir-containing regimen without NS5A inhibitor* with or without compensated cirrhosis: One tablet PO QD for 12 weeks	One tablet (sofosbuvir 400 mg/ velpatasvir 100 mg/ voxilaprevir 100 mg) per day
Vosevi® (sofosbuvir/ velpatasvir/ voxilaprevir)	**Genotype 1-6** treatment-experienced with Vosevi with or without compensated cirrhosis: Vosevi one tablet PO QD with weight-based RBV for 24 weeks	One tablet (sofosbuvir 400 mg/ velpatasvir 100 mg/ voxilaprevir 100 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.
Treatment-experienced refers to previous treatment with NS3 protease inhibitor (telaprevir, boceprevir, or simeprevir) and/or peginterferon/RBV unless otherwise stated.
ǂ *Off-label, AASLD-IDSA guideline-supported dosing regimen*

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	
Sovaldi		Sofosbuvir			
Viekira 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	2-3 mg/dL	Over 3 mg/dL

	1 Point	2 Points	3 Points
	Less than 34 umol/L	34-50 umol/L	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	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: without cirrhosis or with compensated cirrhosis	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD for 12 weeks	Daklinza: 90 mg per day	FDA- approved labeling
Genotype 1: post-liver transplantation in the allograft OR with decompensated cirrhosis	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD with RBV for 12 weeks		
Genotype 3: without cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 12 weeks		
Genotype 3: post-liver	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD		

Indication	Dosing Regimen	Maximum Dose	Reference
transplantation in the allograft OR with compensated cirrhosis or decompensated cirrhosis	with RBV for 12 weeks		

AASLD-IDSA updated guideline no longer supports Daklinza-based regimens.

VI. Product Availability

Tablets: 30 mg, 60 mg, 90 mg

VII. References

1. Daklinza Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; October 2019. Available at http://packageinserts.bms.com/pi/pi_daklinza.pdf. Accessed April 30, 2020.
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 November 6, 2019. Available at: https://www.hcvguidelines.org/. Accessed April 30,2020.
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.	01.17	
Added preferencing for Mavyret; removed preferencing for Epclusa and Harvoni	09.14.17	
Expanded genotypes to reflect AASLD/IDSA CHC treatment guidelines updated April 2017. Initial approval duration expanded to up to full 24 weeks, deleted viral load and adherence requirement in continued therapy section since appropriate full regimen is provided through initial approval duration per specialist feedback to prevent barriers to adherence, added documentation of positive response to therapy and continuity of care. Added section V: dosage and administration	09.14.17	11.17
3Q18 annual review: 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; added requirement for documentation of previous	05.22.18	06.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
treatment and cirrhosis status; 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.		
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.05.19	05.19
3Q 2019 annual review: removed documented sobriety from alcohol and illicit IV drugs for ≥ 6 months prior to starting therapy; references reviewed and updated.	07.02.19	08.19
Via CP.PCH.15: HIM.PA.SP27 retired and combined with Commercial to CP.PCH.15; added requirement that life expectancy ≥ 12 months with HCV treatment and participation in a medication adherence program; 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).	12.03.19	02.20
3Q 2020 annual review: CP.PCH.15 retired and HIM.PA.SP27 unretired per June SDC and prior clinical guidance; updated criteria to remove genotypes 2, 4, 5, and 6 along with dosing section V to reflect that AASLD/IDSA guidelines no longer support Daklinza-based regimens (FDA-labeled indication remains for genotypes 1 and 3 for a 12 week duration); revised authorization duration to 12 weeks from 24 weeks; references reviewed and updated.	06.10.20	08.20

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.

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.

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