Clinical Policy: Daclatasvir (Daklinza)

Reference Number: PA.CP.PHAR.274
Effective Date: 08/17
Last Review Date: 09/17 Revision Log

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

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

Limitation 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
It is the policy of Pennsylvania Health and Wellness® that Daklinza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
*** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria ***

A. Chronic Hepatitis C Infection (must meet all)**:**
1. Age ≥ 18 years;
2. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable HCV RNA (ribonucleic acid) levels;
3. Confirmed HCV genotype is 1, 2, 3, 4, 5, or 6;
4. If actively abusing alcohol or IV drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse and an offer of a referral for substance use disorder treatment.
5. Has all of the following:
   a. Documented quantitative HCV RNA at baseline that was tested within the past 3 months.
   b. Dose not have a life expectancy of less than 12 months due to non-liver-related comorbid conditions.
   c. Has correct or addressed the causes of non-adherence to a previously prescribed Hepatitis C treatment regimen if the recipient has a history of failed treatment due to non-adherence.
   d. Had all potential drug interactions addressed by the prescriber
6. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;
   a. For AASLD-IDSA recommended regimen: If a lower cost alternative regimen carries an equal or higher AASLD-IDSA rating, a clinical contraindication or intolerance must be present for the alternative regimen prior to the approval of a Daklinza-based regimen;

7. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): contraindication or intolerance to Mavyret;or Mavyret is not AASLD recommended.
8. Has a documented commitment to adherence with the planned course of treatment
9. Has documented completion of
    a. Hepatitis B immunization series or Hepatitis B screening (sAb/sAg and cAb/cAg) and
    b. If there is detectable HBV DNA, will be treated for Hepatitis B or if negative for hepatitis BsAb, is being vaccinated against Hepatitis B. and
    c. Has a documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay: Is being treated for HIV or is not being treated for HIV and the medical record documents the rationale for not being treated
10. Member has none of the following contraindications:
    a. Concomitant use of strong inducers of CYP3A, including phenytoin, carbamazepine, rifampin, and St. John's wort;
    b. If Daklinza is prescribed with ribavirin:
        a. Pregnancy or possibility of pregnancy - member or partner;
        b. Hemoglobin < 10 g/dL.
11. For genotype 1a with cirrhosis, laboratory testing confirming the absence of NS5A resistance associated polymorphisms at amino acid positions M28, Q30, L31 and Y93;
12. Prescribed for use in combination with Sovaldi;
13. Dose does not exceed 90 mg (1 tablet) per day.

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

B. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

*** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria ***

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. 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 (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – PA.CP.PHAR.57 or evidence of coverage documents.

IV. Appendices

Appendix A: Abbreviation Key

ALT: alanine aminotransferase
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CTP: Child Turcotte Pugh
DAA: direct acting antiviral
FIB-4: Fibrosis-4 index
HBeAg: hepatitis B virus envelope antigen
HBV: hepatitis B virus
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
IDSA: Infectious Diseases Society of America
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
PI: protease inhibitor
RBV: ribavirin
PO: by mouth
RBV: ribavirin
QD: once per day

Appendix B: General Information

- Hepatitis B Reactivation is a black box warning for all direct-acting antiviral drugs for the treatment of HCV. The provider must provide either:
  - Documentation of absence of concurrent HBV infection as evidenced by laboratory values showing absence of hepatitis B virus envelope antigen (HBeAg) and HBV DNA;
  - Documentation that HBV co-infected patient may not be candidates for therapy as evidenced by one of the following:
    - Absence of HBeAg, HBV DNA less than 2,000 international units/mL, and alanine aminotransferase (ALT) level within 1 to 2 times the upper limit of normal;
    - HBeAg-positive and HBV DNA greater than 1,000,000 international units/mL and ALT level within 1 to 2 times the upper limit of normal;
  - Documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced
- The 2016 AASLD/IDSA treatment guideline for HBV consider ALT levels <30 U/L for men and <19 U/L for women as upper limits of normal.
- The 2016 AASLD/IDSA treatment guideline for HBV recommend adults with compensated cirrhosis, even with low levels of viremia (<2,000 IU/mL) be treated with

antiviral therapy to reduce the risk of decompensation, regardless of ALT level. The recommendation extends to adults with decompensated cirrhosis be treated with antiviral therapy indefinitely regardless of HBV DNA level, HBeAg status, or ALT level to decrease the risk of worsening liver-related complications.

Appendix C: Direct-Acting Antivirals (DAAs) 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			
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs
**Additional PIs no longer recommended: Victrelis (boceprevir), Incivek (telaprevir)

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: 90mg once daily	1) FDA-approved labeling 2) AASLD-04/17)
Genotype 1: Treatment-naïve or treatment-experienced with compensated cirrhosis	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD with or without weight-based RBV for 24 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 1, 4‡, 5‡, or 6‡: 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: 90mg once daily	1) FDA-approved labeling 2) ǂ AASLD-IDSA (updated 04/17)
Genotype 1, 4‡, 5‡, or 6‡: 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: 90mg once daily	ǂ AASLD-IDSA (updated 04/17)

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1 or 4‡: Treatment-naïve or treatment-experienced, post-liver transplantation including those with compensated 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: 90mg once daily	1) FDA-approved labeling 2) ǂ AASLD-IDSA (updated 04/17)
Genotype 1 or 4‡: Treatment -naïve, post-liver transplantation with compensated liver disease, who are ribavirin ineligible	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD for 24 weeks	Daklinza: 90mg once daily	ǂ AASLD-IDSA (updated 04/17)
Genotype 2: Treatment-naïve or treatment-experienced without cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 12 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 2: Treatment -naïve or treatment-experienced with compensated cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 16 to 24 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 2: In whom previous treatment with Sovaldi/RBV has failed	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD with or without weight-based RBV for 24 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 2‡ or 3: Decompensated cirrhosis (including those with hepatocellular carcinoma)	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD with low initial dose of RBV (600 mg) and increased as tolerated for 12 weeks	Daklinza: 90mg once daily	1) FDA-approved labeling 2) ǂ AASLD-IDSA (updated 04/17)
Genotype 2: Treatment-naïve or treatment-experienced, post-liver transplantation, including those with compensated 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: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 2: Treatment -naïve or treatment-experienced, post-liver transplantation, including those with compensated cirrhosis, who are ribavirin ineligible	Daklinza 60 mg PO QD plus Sovaldi 400 mg PO QD for 24 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 3: Treatment-naïve or treatment-experienced with Peg	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 12 weeks	Daklinza: 90mg once daily	1) FDA-approved labeling

Indication	Dosing Regimen	Maximum Dose	Reference
IFN/RBV without cirrhosis			2) AASLD-IDSA (updated 04/17)
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: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 3: Treatment-experienced with Peg IFN/RBV or with sofosbuvir-based treatment without prior experience with NS5A inhibitor with compensated cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD with weight-based RBV for 24 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 3: In whom previous treatment with Sovaldi/RBV has failed	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD with weight-based RBV for 24 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 3: Treatment-naïve or treatment-experienced, post-liver transplantation, in the allograft, including those with compensated cirrhosis	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD with low initial dose RBV (600mg, increased as tolerated) for 12 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17)
Genotype 3: Treatment-naïve or treatment-experienced, post-liver transplantation, in the allograft, including those with compensated cirrhosis, who are ribavirin ineligible	Daklinza 60 mg PO plus Sovaldi 400 mg PO QD for 24 weeks	Daklinza: 90mg once daily	AASLD-IDSA (updated 04/17
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: 90mg once daily	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.*

ǂ *Off-label, AASLD-IDSA guideline-supported dosing regimen*

VI. Product Availability

Tablet: 30 mg, 60 mg, 90mg

Reviews, Revisions, and Approvals	Date	Approval Date
Policy converted to new template. Added requirement for prevention of HBV reactivation; expanded genotypes to reflect AASLD/IDSA CHC treatment guidelines. Consolidated appendix D and E into dosing and administration in section V; added maximum dose requirement; initial approval duration expanded to full 12 weeks, limited continued therapy approval duration to 12 weeks, deleted viral load and adherence requirement in continued therapy, added documentation of positive response to therapy and continuity of care, and removed CIs in section II, added reference column in section V. Added preferencing information requiring Mavyret for FDA-approved indications. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by 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	09/17

References

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