Clinical Policy: Daclatasvir (Daklinza)

Reference Number: NV.PHAR.274
Effective Date: 07/17
Last Review Date: 01/19

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

Description
Daklinza™ (daclatasvir) is an inhibitor of HCV nonstructural protein 5A (NS5A) and is a direct-acting antiviral (DAA) agent against the hepatitis C virus.

FDA Approved Indications
Daklinza is an HCV NS5A inhibitor/oral tablet formulation indicated for use with sofosbuvir, with or without ribavirin, for:

- Treatment of patients with chronic HCV genotype 1, 2, or 3.
- Limitations of use: Sustained virologic response (SVR12) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) to support that the member has met all approval criteria.

It is the policy of SilverSummit Healthplan that Daklinza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Hepatitis C Infection (must meet all)

1. Age ≥ 18 years;
2. Diagnosis of chronic HCV infection as evidenced by detectable HCV RNA (ribonucleic acid) levels over a six (6) month period;
3. Confirmed HCV genotype is 1, 2, 3, 4, 5 or 6;
4. Life expectancy ≥ 12 months with HCV treatment;
5. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section IV Dosage and Administration*);
6. If cirrhosis is present, confirmation of Child-Pugh A status;
7. Member is hepatitis B virus (HBV) negative, or if positive, documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
8. Member agrees to participate in a medication adherence program meeting both of the following components:
   a. Medication adherence monitored by pharmacy claims data or member report, and
   b. Member's risk for non-adherence identified by adherence program or member/prescribing physician follow-up at least every four (4) weeks; and
9. Member has contraindication or intolerance to the following preferred medication(s)

a. For genotype 1: Mavyret and Zepatier *(Mavyret is the preferred agent; Zepatier should be used if Mavyret is contraindicated);and*
b. For genotype 2 and 3: Epclusa.

Approval Duration: Up to a Total of 24 Weeks*
*(*Approved duration should be consistent with a regimen in *Section IV Dosage and Administration)*

B. Other Diagnoses/Indications
Refer to CP.PMN.53 if diagnosis is NOT specifically listed under *Section III Diagnoses/Indications for Which Coverage is NOT Authorized*.

II. Continued Therapy

A. Chronic Hepatitis C Infection (must meet all)
1. Currently receiving medication via SilverSummit Healthplan benefit;
2. Member is responding positively to therapy, (e.g., decreased HCV RNA level, no unacceptable toxicity);
3. All requirements stated in the most current version of the Nevada Division of Health Care Financing and Policy's (DHCFP) Medicaid Services Manual, Chapter 1200 (MSM 1200) have been/are being met; and
4. Recipient is compliant on all drugs in treatment regimen

Approval Duration: Up to a Total of 24 Weeks*
*(*Approved duration should be consistent with a regimen in *Section IV Dosage and Administration)*

B. Other Diagnoses/Indications (must meet 1 or 2)
1. Currently receiving medication via SilverSummit Healthplan benefit and documentation supports positive response to therapy, or
2. Refer to CP.PMN.53.

III. Diagnoses/Indications for Which Coverage is NOT Authorized:

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 – CP.PMN.53 or evidence of coverage documents.

IV. Dosage and Administration

FDA-Approved Regimens and Treatment Durations

Dose is one of the following:
60 mg (one tablet) daily; or
30 mg (one tablet) and the recipient is receiving a strong CYP3A inhibitor; or
90 mg (one tablet) daily and the recipient is receiving a concomitant moderate CYP3A inducer.

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
No Cirrhosis or Compensated Cirrhosis (CTP/Child-Pugh Class A)			
Not specified	1*, 3	Not specified	Sovaldi + Daklinza§
Decompensated Cirrhosis (CTP/Child-Pugh Class B or C)			
Not specified	1*, 3	Not specified	Sovaldi + Daklinza + RBV§
Post-Transplantation			
Not specified	3	Not specified	Sovaldi + Daklinza + RBV§

*Subtype a or b, or unknown subtype
§Treatment duration - 12 weeks

AASLD-IDSA Recommended Regimens and Treatment Durations

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
No Cirrhosis			
Treatment naive	1*, 2, 3, 4	None	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
	1a, 1b, 2, 3	None	Sovaldi + Daklinza§
	2, 3	None	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
Treatment experienced	1*	NS3 PI/Peg-IFN/RBV**	Sovaldi + Daklinza§
	1*, 2, 3, 4	Not specified	Sovaldi + Daklinza + RBV§ *If post-liver transplantation.*
	1a, 1b, 2, 3	Peg-IFN/RBV	Sovaldi + Daklinza§
	2, 3	Not specified	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
	3	Sovaldi/RBV	Sovaldi + Daklinza + RBV†
Compensated Cirrhosis (CTP/Child-Pugh Class A)			
Treatment naive	1*, 2, 3, 4	None	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
	1*, 4	None	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
	1a, 1b	None	Sovaldi + Daklinza +/- RBV†
	2	None	Sovaldi + Daklinza◊
	2, 3	None	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*

Treatment Naive/Experienced	Genotype	Failed Treatment Regimen	Recommended Regimen *See footnotes for duration*
	3	None	Sovaldi + Daklinza†
Treatment experienced	1*	NS3 PI/Peg-IFN/RBV**	Sovaldi + Daklinza + RBV†
	1*, 2, 3, 4	Not specified	Sovaldi + Daklinza + RBV§ *If post-liver transplantation.*
	1a, 1b	Peg-IFN/RBV	Sovaldi + Daklinza +/- RBV†
	2	Peg-IFN/RBV	Sovaldi + Daklinza◊
		Sovaldi/RBV	Sovaldi + Daklinza†
	2, 3	Not specified	Sovaldi + Daklinza† *If post-liver transplantation and RBV ineligible.*
	3	Sovaldi/RBV	Sovaldi + Daklinza + RBV†
		Peg-IFN/RBV	Sovaldi + Daklinza + RBV†
Decompensated Cirrhosis (CTP/Child-Pugh Class B or C)			
Treatment naive	1*, 4	None	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
Treatment experienced	1*, 4	Not specified	Sovaldi + Daklinza +RBV§ *If post-liver transplantation.*
Not specified	1*, 2, 3, 4	Not specified	Sovaldi + Daklinza + RBV*
	1*, 4	Not specified	Sovaldi + Daklinza† *If RBV ineligible.*

*Subtype a or b, or unknown subtype
**NS3 includes Victrelis (boceprevir), Incivek (telaprevir) or Olysio (simeprevir)
§Treatment duration - 12 weeks
◊ Treatment duration – 16 to 24 weeks
†Treatment duration - 24 weeks

V. Product Availability

Tablet, Oral Daklinza: 30 mg, 60 mg, 90 mg
Capsule, Oral:

- Rebetol: 200 mg
- Ribasphere: 200 mg
- Generic: 200 mg

Solution, Oral:

- Rebetol: 40 mg/mL (100 mL)

Tablet, Oral:

- Copegus: 200 mg
- Moderiba (includes dose packs): 200 mg, 400 mg, 600 mg
- Ribasphere: 200 mg, 400 mg, 600 mg
- Ribasphere RibaPak (dose packs): 200 mg, 400 mg, 600 mg
- Generic: 200 mg

VI. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

- 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
- 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

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 one (1) of the following:
  - Documentation of absence of concurrent HBV infection as evidenced by laboratory values showing absence of hepatitis B virus envelope antigen (HBeAg) and HBV DNA (deoxyribonucleic acid); or
  - 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 one (1) to two (2) times the upper limit of normal; or
    - HBeAg-positive and HBV DNA greater than 1,000,000 international units/mL and ALT level within one (1) to two (2) times the upper limit of normal; or
  - Documentation that concurrent HBV infection is being treated (e.g., tenofovir alafenamide, adefovir, entecavir), unless contraindicated or clinically significant adverse effects are experienced.
- Due to higher rates of virologic failure and treatment-emergent drug resistance, the data does not support labeling for treatment of HCV genotype 1 infected patients who are both NS3/4A PI and NS5A inhibitor-experienced.

Appendix C. 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			
Olysio				Simeprevir	

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)**	CYP3A Inhibitor
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)

VII. References

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12. Ribavirin (systemic): Drug information. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed July 11, 2016.

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. SilverSummit Healthplan 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. "Healthplan" means the SilverSummit Healthplan which has adopted this clinical policy and that is operated or administered, in whole or in part, by SilverSummit Healthplan or any of such Healthplan'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 Healthplan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Healthplan. 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 Healthplan 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 Healthplan has no control or right of control. Providers are not agents or employees of the Healthplan.

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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 Medicaid members, when State Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, State Medicaid coverage provisions take precedence. Please refer to the State Medicaid Manual (MSM 1200, revised August 1, 2017) for any coverage provisions pertaining to this clinical policy. The Medicaid Manual may be located at the Nevada Department of Health and Human Services Division of Health Care Financing and Policy (DHCFP) at http://dhcfp.nv.gov/Resources/AdminSupport/Manuals/MSM/C1200/Chapter1200/.

Revision Log

Reviews, Revisions, and Approvals	Date	Approval Date
New policy created for SilverSummit based on Nevada requirements Policy revised with standard formatting and current (August 1, 2017) MSM 1200 information	02/17 12/17	07/17
Q1 2019 annual review; expanded HCV genotype to include 1, 2, 3, 4, 5, or 6	01/19	01/08/2019