



Louisiana

Treatment of Hepatitis C with daclatasvir (Daklinza™) plus sofosbuvir (Sovaldi®)

Policy # 00479

Original Effective Date: 12/16/2015

Current Effective Date: 11/21/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Treatment of Hepatitis C with Dual Therapy (Ribavirin Plus Pegylated Interferon Alfa) is addressed separately in medical policy 00374.

Note: Pegylated Interferons (Pegasys®, PegIntron®)† for Other (Non-Hepatitis C) Uses is addressed separately in medical policy 00375.

Note: Treatment of Hepatitis C with a sofosbuvir (Sovaldi®)†Based Regimen is addressed separately in medical policy 00397.

Note: Treatment of Hepatitis C with sofosbuvir/ledipasvir (Harvoni®)† is addressed separately in medical policy 00455.

Note: Treatment of Hepatitis C with simeprevir (Olysio®)† PLUS sofosbuvir (Sovaldi®)† is addressed separately in medical policy 00457.

Note: Treatment of Hepatitis C with ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak®)† is addressed separately in medical policy 00462.

Note: Treatment of Hepatitis C with ombitasvir, paritaprevir, and ritonavir (Technivie®)† is addressed separately in medical policy 00478.

Note: Treatment of Hepatitis C with elbasvir and grazoprevir (Zepatier™)† is addressed separately in medical policy 00509.

Note: Treatment of Hepatitis C with sofosbuvir and velpatasvir (Epclusa®)† is addressed separately in medical policy 00514.

Note: Treatment of Hepatitis C with glecaprevir/pibrentasvir (Mavyret®)† is addressed separately in medical policy 00593.

Note: Treatment of Hepatitis C with sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)† is addressed separately in medical policy 00594

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When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member's contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider daclatasvir (Daklinza™)† plus sofosbuvir (Sovaldi®)† for the treatment of individuals with chronic hepatitis C virus (HCV) to be **eligible for coverage**.

Genotype 1

Patient Selection Criteria

Based on review of available data, the Company may consider daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) for the treatment of genotype 1 chronic hepatitis C virus (HCV) when the following criteria are met:

- Patient has a diagnosis of chronic hepatitis C virus (HCV) genotype 1; AND
- Daklinza will be used in combination with Sovaldi; AND
- Patient has NOT failed prior therapy with drugs such as elbasvir/grazoprevir (Zepatier™)†, sofosbuvir/ledipasvir (Harvoni®)†, sofosbuvir/velpatasvir (Epclusa®)†, ombitasvir, paritaprevir, ritonavir, dasabuvir (Viekira Pak®)†, daclatasvir (Daklinza™)†, sofosbuvir (Sovaldi®)†, or ombitasvir, paritaprevir, ritonavir (Technivie®)†; AND
- There is clinical evidence or patient history suggests the use of sofosbuvir/velpatasvir (Epclusa), sofosbuvir/ledipasvir (Harvoni), or glecaprevir/pibrentasvir (Mavyret) will be ineffective or will cause an adverse reaction to the patient; AND
*Note that this criterion is an additional company requirement. Failure to meet this criterion will result in a denial of not medically necessary.***
- Daklinza (if approved) will be used as follows:

Scenario	Cirrhotic/Non-Cirrhotic	Drugs	Length of Therapy
Tx naïve	Non-Cirrhotic	Daklinza Plus Sovaldi	12 weeks
Tx naïve	Compensated Cirrhosis	Daklinza Plus Sovaldi with or without ribavirin	24 weeks [ⓧ]
Tx experienced (pegylated interferon plus ribavirin)	Non-Cirrhotic	Daklinza Plus Sovaldi	12 weeks
Tx experienced (pegylated interferon plus ribavirin)	Compensated Cirrhosis	Daklinza Plus Sovaldi with or without ribavirin	24 weeks [ⓧ]
Tx experienced [telaprevir (Incivek™)†, boceprevir (Victrelis®)†, or simeprevir (Olysio®)† PLUS pegylated	Non-cirrhotic	Daklinza Plus Sovaldi	12 weeks

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interferon plus ribavirin]			
Tx experienced [telaprevir (Incivek), boceprevir (Victrelis), or simeprevir (Olysio) PLUS pegylated interferon plus ribavirin]	Compensated Cirrhosis	Daklinza Plus Sovaldi with or without ribavirin	24 weeks ^{&}
Any	Decompensated Cirrhosis	Daklinza Plus Sovaldi Plus ribavirin	12 weeks
Post-Transplant	N/A	Daklinza Plus Sovaldi Plus ribavirin	12 weeks

[&]These regimens are considered "off-label" however they are mentioned in the AASLD (American Association for the Study of Liver Diseases) Hepatitis C Guidelines. If the requirements for the addition of ribavirin or the requirement of 24 weeks of therapy is not met, these will be denied as not medically necessary** as they are a requirement beyond the package insert.

Table Definitions:

Compensated Cirrhosis (Child-Pugh A):

- Metavir Stage 4; or
- Ishak score of 5 or 6; or
- FibroTest/FibroSure score of more than 0.75; or
- APRI of greater than 2; or
- FibroScan results greater than 12.5kPA.

Decompensated Cirrhosis (Child Pugh B/C)

When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) for any time frame other than 24 weeks in patients that have genotype 1 hepatitis C virus (HCV) with compensated cirrhosis and are treatment naïve/have failed therapy with pegylated interferon PLUS ribavirin OR telaprevir (Incivek), boceprevir (Victrelis), or simeprevir (Olysio) PLUS pegylated interferon PLUS ribavirin to be **not medically necessary.****

Based on review on available data, the Company considers the use of daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) WITHOUT clinical evidence or patient history that suggests the use of sofosbuvir/velpatasvir (Epclusa), sofosbuvir/ledipasvir (Harvoni), or glecaprevir/pibrentasvir (Mavyret) in patients with genotype 1 hepatitis C virus (HCV) will be ineffective or will cause an adverse reaction to the patient to be **not medically necessary.****

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of daclatasvir (Daklinza) plus sofosbuvir (Sofaldi) when patient selection criteria are not met (with the exception of the criterion denoted above as **not medically necessary****) to be **investigational.***

Genotype 3

Patient Selection Criteria

Based on review of available data, the Company may consider daclatasvir (Daklinza) plus sofosbuvir (Sofaldi) for the treatment of genotype 3 chronic hepatitis C virus (HCV) when the following criteria are met:

- Patient has a diagnosis of chronic hepatitis C virus (HCV) genotype 3; AND
- Daklinza will be used in combination with Sofaldi; AND
- Patient has not failed a daclatasvir (Daklinza) containing regimen; AND
- There is clinical evidence or patient history suggesting that sofosbuvir/velpatasvir (Epclusa®)† or glecaprevir/pibrentasvir (Mavyret) will be ineffective or will cause an adverse reaction to the patient; AND

*Note that this criterion is an additional company requirement. Failure to meet this criterion will result in a denial of not medically necessary.***

- Daklinza (if approved) will be used as follows:

Scenario	Cirrhotic/Non-Cirrhotic	Drugs	Length of Therapy
Tx naïve	Non-Cirrhotic	Daklinza Plus Sofaldi	12 weeks
Tx naïve	Compensated Cirrhosis	Daklinza Plus Sofaldi with or without Ribavirin	24 weeks [ⓧ]
Tx experienced (pegylated interferon plus ribavirin)	Non-Cirrhotic	Daklinza Plus Sofaldi	12 weeks
Tx experienced (pegylated interferon plus ribavirin)	Compensated Cirrhosis	Daklinza Plus Sofaldi Plus Ribavirin	24 weeks [ⓧ]
Tx experienced (Sofaldi plus ribavirin)	Non-cirrhotic OR Compensated Cirrhosis	Daklinza Plus Sofaldi Plus Ribavirin	24 weeks [ⓧ]
Any	Decompensated Cirrhosis	Daklinza Plus Sofaldi Plus Ribavirin	12 weeks
Post Liver Transplant	N/A	Daklinza Plus Sofaldi Plus Ribavirin	12 weeks

[ⓧ]These regimens are considered "off-label" however they are mentioned in the AASLD (American Association for the Study of Liver Diseases) Hepatitis C Guidelines. If the requirements for the addition of

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*ribavirin or the requirement of 24 weeks of therapy is not met, these will be denied as not medically necessary** as they are a requirement beyond the package insert.*

Table Definitions:

Compensated Cirrhosis (Child Pugh A):

- Metavir Stage 4; or
- Ishak score of 5 or 6; or
- FibroTest/FibroSure score of more than 0.75; or
- APRI of greater than 2; or
- FibroScan results greater than 12.5kPA.

Decompensated Cirrhosis (Child Pugh B/C)

When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) for any time frame other than 24 weeks in patients with genotype 3 hepatitis C virus (HCV) that have compensated cirrhosis or have failed a sofosbuvir (Sovaldi) containing regimen to be **not medically necessary.****

Based on review on available data, the Company considers the use of daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) without the addition of ribavirin in hepatitis C virus (HCV) genotype 3 patients that have compensated cirrhosis (where required) or have failed a sofosbuvir (Sovaldi) containing regimen to be **not medically necessary.****

Based on review on available data, the Company considers the use of daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) WITHOUT clinical evidence or patient history that suggests sofosbuvir/velpatasvir (Epclusa) or glecaprevir/pibrentasvir (Mavyret) in patients with genotype 3 hepatitis C virus (HCV) will be ineffective or will cause an adverse reaction to the patient to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) when patient selection criteria are not met (with the exception of the criterion denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Daklinza is a HCV NS5A inhibitor indicated for use along with Sovaldi for the treatment of chronic HCV genotypes 1 and 3. Daklinza is supplied in 60mg, 30mg, and 90mg tablets, and there are dose modifications involved for concomitant use with CYP3A inhibitors and inducers. The recommended dose of

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Daklinza is a 60mg tablet taken once daily (with or without food) in combination with Sovaldi for 12 weeks. The package insert notes that cure rates are not as high in cirrhotic patients as they are in non-cirrhotic patients. This is likely why guidelines support 24 weeks of therapy in patients with cirrhosis.

Hepatitis C

Hepatitis C is the most common blood borne pathogen. In the US, there are approximately 5.2 million people chronically infected with hepatitis C. Hepatitis C, a single-stranded ribonucleic acid (RNA) virus, is genetically complex with several recognized genotypes. Genotypes 1, 2, and 3 are the most frequently encountered genotypes worldwide.

Drug regimens have evolved quite a bit over the past few years in this class. It is beyond the scope of this policy to delve into the entire timeline of approvals, however a brief overview will provide an idea of the evolution of these drugs. The earlier regimens contained ribavirin and interferon/pegylated interferons. The next wave of products brought NS3/4A protease inhibitors to market such as Incivek and Victrelis. After that, an NS5B polymerase inhibitor was approved (Sovaldi). Following the release of Sovaldi, a drug was approved that contained a combination NS5A inhibitor and NS5B polymerase inhibitor combination (Harvoni). Drugs approved up until that point in time mainly treated genotype 1 HCV. After these drugs were approved, a multitude of other drugs were approved (Viekira/XR, Zepatier, Daklinza, etc). As drugs continue to be FDA approved in this space, the range of genotypes that can be treated increases. The latest wave of drugs includes pangenotypic products such as Eplcusa, Mavyret, and Vosevi. For more information on each individual drug, please see the product's package insert or refer to their respective medical policy.

Daklinza has been integrated into the AASLD guidelines in various scenarios for the treatment of HCV, however it should be noted that these guidelines are receiving constant updates as new products are approved.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Daklinza was approved in July of 2015 for use along with Sovaldi for the treatment of chronic HCV genotype 3 infection. In April of 2016, Daklinza was approved (along with Sovaldi) to treat patients with HCV genotype 1 infections.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Daklinza in combination with Sovaldi were evaluated in a phase 3 open label trial that included 152 subjects with chronic HCV genotype 3 infection and compensated liver disease who were

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treatment naïve or treatment experienced. Most treatment experienced patients had been treated with pegylated interferon and ribavirin, but 7 subjects had been treated with a sofosbuvir regimen and 2 subjects with an investigational regimen. Subjects received Daklinza 60 mg plus Sovaldi 400 mg once daily for 12 weeks and were monitored for 24 weeks post treatment. The primary endpoint was the percentage of patients achieving SVR at 12 weeks. In treatment naïve subjects without cirrhosis, 98% of patients achieved an SVR12 compared to 58% of patients with cirrhosis achieving an SVR12. In treatment experienced patients without cirrhosis, 92% of patients achieved an SVR12 compared to 69% of patients with cirrhosis achieving an SVR12. The outcomes in those with cirrhosis are less favorable than those without cirrhosis.

Daklinza in combination with Sovaldi was also studied in a trial mainly focusing on genotype 1 and 3 subjects that were treatment naïve or treatment experienced, with or without cirrhosis, and human immunodeficiency syndrome (HIV)/HCV coinfectd. In genotype 1 patients, the SVR12 overall was 97%. For those without cirrhosis, the SVR12 was 98%, and in those with cirrhosis, the SVR12 was 91%. There were 127 total subjects with genotypes 1 and 3 in this study. A separate trial included subjects with genotypes 1 or 3, treatment naïve or treatment experienced, with or without cirrhosis, including decompensated cirrhosis and post-transplant. The overall SVR12 was 82%, 91% for Child Pugh A, 92% for Child Pugh B, 50% for Child Pugh C, and 95% for post liver transplant.

References

1. Daklinza. [package insert]. Bristol Myers Squibb Company. Princeton, NJ.
2. Recommendations for Testing, Managing, and Treating Hepatitis C. American Association for the Study of liver diseases. Updated July 2016.
3. Veteran's Affairs chart for interferon ineligibility: <http://www.hepatitis.va.gov/provider/guidelines/2014hcv/tables.asp>. Accessed September 2017.

Policy History

Original Effective Date: 12/16/2015

Current Effective Date: 11/21/2018

12/03/2015 Medical Policy Committee review

12/16/2015 Medical Policy Implementation Committee approval. New Policy

08/04/2016 Medical Policy Committee review

08/17/2016 Medical Policy Implementation Committee approval. Added indication for genotype 1. For genotype 3, switched out preference of Sovaldi plus ribavirin plus pegylated interferon to instead use Epclusa prior to Daklinza plus Sovaldi. Updated relevant background information.

08/03/2017 Medical Policy Committee review

08/23/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

11/02/2017 Medical Policy Committee review

11/15/2017 Medical Policy Implementation Committee approval. Changed from Harvoni first to Epclusa, Harvoni, or Mavyret first for genotype 1. Changed from Epclusa first to Epclusa or Mavyret first for genotype 3.

12/20/2017 Adjustment made to title of policy.

11/08/2018 Medical Policy Committee review

11/21/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 11/2019

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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