Treatment of Hepatitis C with a sofosbuvir (Sovaldi®) Based Regimen

Policy # 00397
Original Effective Date: 01/15/2014
Current Effective Date: 11/13/2023

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 sofosbuvir/ledipasvir (Harvoni®, Authorized Generic) is addressed separately in medical policy 00455.

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 elbasvir and grazoprevir (Zepatier™) is addressed separately in medical policy 00509.

Note: Treatment of Hepatitis C with sofosbuvir/velpatasvir (Epclusa®, Authorized Generic) 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.

When Services May Be Eligible for Coverage

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

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

Chronic Hepatitis C Virus

Based on review of available data, the Company may consider a sofosbuvir (Sovaldi®)‡ based regimen (including ribavirin or ribavirin + pegylated interferon alfa) for the treatment of individuals with chronic hepatitis C virus (HCV) to be **eligible for coverage.****

Patient Selection Criteria

Based on review of available data, the Company may consider the use of a sofosbuvir (Sovaldi) based regimen (including ribavirin or ribavirin + pegylated interferon alfa) when ALL of the following criteria are met:

- Requested drug must NOT be used as monotherapy; AND
- Patient does NOT have decompensated cirrhosis; AND
- Patient has NOT used a sofosbuvir containing regimen in the past [e.g., Sovaldi, Harvoni®‡ (or its authorized generic), Epclusa®‡ (or its authorized generic), Vosevi™‡‡]; AND
- Patient has diagnosis of chronic hepatitis C virus Genotypes 1, 2, 3, or 4, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with hepatitis C virus/human immunodeficiency virus (HIV-1) co-infection; AND
- Patient meets ONE of the following conditions:
    - Patients with genotype 1 hepatitis C virus must receive concurrent therapy with pegylated interferon alfa and ribavirin; OR
    - Patients with genotype 1 hepatitis C virus must receive concurrent therapy with ribavirin alone if they are interferon ineligible ONLY when there is clinical evidence or patient history that suggests the use of the clinically applicable preferred products [i.e.,sofosbuvir/velpatasvir (Epclusa), sofosbuvir/ledipasvir (Harvoni)] will be ineffective or will cause an adverse reaction to the patient; OR
      *(Note: This specific patient criterion [requiring use of Harvoni and Epclusa] is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
    - Patients with genotype 2 or 3 hepatitis C virus must receive concurrent therapy with ribavirin; OR

- Patients with genotype 4 hepatitis C virus must receive concurrent therapy with pegylated interferon alfa and ribavirin; OR
- Patients with hepatocellular carcinoma awaiting liver transplantation must receive concurrent therapy with ribavirin; AND

- Patient meets the following definitions and adheres to the timeframes for treatment:

HCV Mono-infected and HCV/HIV-1 Co-infected	**Drugs**	**Duration**
Genotype 1 or 4	Sovaldi + pegylated interferon alfa + ribavirin	12 weeks
Genotype 1 interferon ineligible	Sovaldi + ribavirin	24 weeks
Genotype 2	Sovaldi + ribavirin	12 weeks
Genotype 3	Sovaldi + ribavirin	24 weeks
Hepatocellular carcinoma	Sovaldi + ribavirin	48 weeks or until liver transplantation, whichever occurs first

When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of sofosbuvir (Sovaldi) and ribavirin for 24 weeks in genotype 1 interferon ineligible patients WITHOUT clinical evidence or patient history that suggests the use of the clinically applicable preferred products [i.e.,sofosbuvir/velpatasvir (Epclusa), sofosbuvir/ledipasvir (Harvoni)] 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 a sofosbuvir (Sovaldi) based regimen (including ribavirin or ribavirin + pegylated interferon alfa) for the treatment of individuals

with chronic hepatitis C virus when patient selection criteria are not met (with the exception of the criterion denoted above as **not medically necessary****) to be **investigational.***

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.*

Other Uses

Based on review of available data, the Company may consider sofosbuvir (Sovaldi) + pegylated interferon alfa + ribavirin for the treatment of individuals with chronic hepatitis C virus to be **eligible for coverage.****

Patient Selection Criteria

Based on review of available data, the Company may consider the use of sofosbuvir (Sovaldi) + pegylated interferon alfa + ribavirin when ALL of the following criteria are met:

- Patient has a diagnosis of chronic hepatitis C virus genotype 3; AND
- Requested drug must NOT be used as monotherapy; AND
- Patient does NOT have decompensated cirrhosis; AND
- Patient meets the following definitions and adheres to the timeframes for treatment:

Clinical Scenario	Drugs	Duration
Genotype 3: treatment naïve/experienced, cirrhotic/non-cirrhotic	Sovaldi + pegylated interferon alfa + ribavirin	12 weeks

*Note that failure to meet the additional company timeframe requirement of 12 weeks for treatment with Sovaldi + pegylated interferon alfa + ribavirin will result in a denial of not medically necessary.***

Treatment experienced for this section: defined as a patient that has failed treatment (i.e., null responder, partial responder, relapser) with either peginterferon alfa plus ribavirin OR a sofosbuvir (Sovaldi) containing regimen.

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When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of sofosbuvir (Sovaldi) + pegylated interferon alfa + ribavirin for any timeframe other than 12 weeks in genotype 3 patients 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 sofosbuvir (Sovaldi) + pegylated interferon alfa + ribavirin for the treatment of individuals with chronic hepatitis C virus when patient selection criteria are not met (with the exception of the criterion denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Sovaldi is a HCV nucleotide analog NS5B polymerase inhibitor indicated for the treatment of chronic hepatitis C virus infection as a component of a combination antiviral treatment regimen. Sovaldi's efficacy has been established in subjects with HCV genotype 1, 2, 3 or 4 infection, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection. Sovaldi should be used in combination with ribavirin or in combination with pegylated interferon and ribavirin, depending on the patient scenario. The manufacturer of Sovaldi did not seek an additional indication for use with Olysio®‡, and therefore the label is unlikely to change. Bristol Myers Squibb also gained an indication for its product, Daklinza™‡, in combination with Sovaldi. Daklinza is no longer commercially available.

Hepatitis C

Hepatitis C is the most common blood borne pathogen. In the US, there are approximately 3.2 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. Type 1a is most frequently found in Northern Europe and North America, while 1b is most common in Japan and Southern and Eastern Europe. Genotypes 4 and 5 are most commonly found in Africa, while genotype 6 is common in Asia.

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 hepatitis C virus. After these drugs were approved, a multitude of other drugs were approved (Viekira/XR®‡, Zepatier™‡, Daklinza, etc). As drugs continue to be U.S. Food and Drug Administration (FDA) approved in this space, the range of genotypes that can be treated increases. The latest wave of drugs includes pan-genotypic products such as Epclusa, Mavyret™‡, and Vosevi™‡. For more information on each individual drug, please see the product's package insert or refer to their respective medical policy.

Sovaldi, as a single entity agent, is no longer recommended in the AASLD (American Association for the Study of Liver Diseases) guidelines as a mainstay of therapy. Sofosbuvir, as part of other drugs (e.g., Epclusa, Harvoni, Vosevi) has been integrated into the guidelines in various situations. 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)

Sovaldi was approved in December of 2013 and is indicated for the treatment of CHC genotype 1-4 as a component of a combination antiviral treatment regimen. Sovaldi is also approved in patients 3 years of age and older with genotype 2 or 3 chronic hepatitis C virus infection without cirrhosis or with compensated cirrhosis in combination with ribavirin.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Sovaldi was evaluated in five Phase 3 trials in a total of 1,724 hepatitis C virus (HCV) mono-infected subjects with genotypes 1 to 6 chronic hepatitis C (CHC) and one Phase 3 trial in 223 HCV/HIV-1 co-infected subjects with genotype 1, 2 or 3 CHC. Among the five trials in HCV mono-infected subjects, one was conducted in treatment-naïve subjects with genotype 1, 4, 5 or 6 CHC in combination with peginterferon alfa 2a and ribavirin and the other four were conducted in subjects with genotype 2 or 3 CHC in combination with ribavirin, including one in treatment-naïve subjects, one in interferon intolerant, ineligible or unwilling subjects, one in subjects previously treated with an interferon-based regimen, and one in all subjects irrespective of prior treatment history or ability to take interferon. The trial in HCV/HIV-1 co-infected subjects was conducted in combination with ribavirin in treatment-naïve subjects with genotype 1 CHC and all subjects with genotype 2 or 3 CHC irrespective of prior treatment history or ability to take interferon. Subjects in these trials had compensated liver disease including cirrhosis. Sovaldi was administered at a dose of 400 mg once daily. The ribavirin dose was weight-based at 1000-1200 mg daily administered in two divided doses when used in combination with Sovaldi, and the peginterferon alfa 2a dose, where applicable, was 180 micrograms per week. Treatment duration was fixed in each trial and was not guided by subjects' HCV RNA levels (no response guided algorithm). Plasma HCV RNA values were measured during the clinical trials using the COBAS TaqMan HCV test (version 2.0), for use with the High Pure System. The assay had a lower limit of quantification (LLOQ) of 25 IU per mL. Sustained virologic response was the primary endpoint which was defined as HCV RNA less than LLOQ at 12 weeks after the end of treatment.

Treatment Naïve Adults Genotype 1 or 4

NEUTRINO was an open-label, single-arm trial that evaluated 12 weeks of treatment with Sovaldi in combination with peginterferon alfa 2a and ribavirin in treatment-naïve subjects with genotype 1, 4, 5 or 6 HCV infection compared to pre-specified historical control. There were 327 treated subjects in this trial. The response was represented by sustained virologic response (SVR) at 12 weeks, also known as SVR12. Overall SVR12 for the treatment group was 90% and varied by genotype. No patients in the treatment group had a virologic failure while 9% of the subjects experienced a relapse. One percent (1%) of patients were lost to follow-up.

Treatment Naïve Adults Genotype 2 or 3

FISSION was a randomized, open-label, active-controlled trial that evaluated 12 weeks of treatment with Sovaldi and ribavirin compared to 24 weeks of treatment with peginterferon alfa 2a and ribavirin in treatment-naïve subjects with genotype 2 and 3 HCV. The ribavirin doses used in the

Sovaldi + ribavirin and peginterferon alfa 2a + ribavirin arms were weight-based 1000-1200 mg per day and 800 mg per day regardless of weight, respectively. Subjects were randomized in a 1:1 ratio and stratified by cirrhosis (presence vs. absence), HCV genotype (2 vs. 3) and baseline HCV RNA level (< 6 log10 IU/mL vs. ≥ 6 log 10 IU/mL). Subjects with genotype 2 or 3 HCV were enrolled in an approximately 1:3 ratio. There were 256 members in the Sovaldi + ribavirin group and 243 members in the peginterferon alfa 2a + ribavirin group. The response was represented by SVR at 12 weeks, also known as SVR12. Overall SVR12 for the 2 genotypes combined was 67% in each of the groups. For genotype 2, 95% of patients in the Sovaldi + ribavirin group achieved an SVR 12 vs. 78% in the peginterferon alfa 2a + ribavirin group. For genotype 3, 56% of patients in the Sovaldi + ribavirin group achieved an SVR 12 vs.63% in the peginterferon alfa 2a + ribavirin group. There was a less than 1% virologic failure rate in the Sovaldi + ribavirin group vs. a 7% rate in the peginterferon alfa 2a + ribavirin group. The relapse rate for the Sovaldi + ribavirin group was 5% vs. 15% in the peginterferon alfa 2a + ribavirin group in patients with genotype 2 HCV. In patients with genotype 3 HCV, there was a 40% relapse rate in the Sovaldi + ribavirin group vs. 24% in the peginterferon alfa 2a + ribavirin group. Breakouts for cirrhosis patients are located in the package insert.

Interferon Intolerant, Ineligible, or Unwilling Adults with Genotype 2 or 3
POSITRON was a randomized, double-blinded, placebo-controlled trial that evaluated 12 weeks of treatment with Sovaldi and ribavirin (N = 207) compared to placebo (N = 71) in subjects who are interferon intolerant, ineligible or unwilling. Subjects were randomized in 3:1 ratio and stratified by cirrhosis (presence vs. absence). The response was represented by SVR at 12 weeks, also known as SVR12. The overall SVR12 for the treated group was 78%. This breaks down to 93% SVR 12 in genotype 2 patients and 61% SVR in genotype 3 patients. There were no virologic failures in the treated group. The relapse rate for the treated group was 5% in those with genotype 2 and 38% in those with genotype 3. None of the patients in the placebo group achieved SVR12. More data regarding a cirrhosis breakout and interferon classification is available in the package insert.

Previously Treated Adults with Genotype 2 or 3
FUSION was a randomized, double-blinded trial that evaluated 12 or 16 weeks of treatment with Sovaldi and ribavirin in subjects who did not achieve SVR with prior interferon-based treatment (relapsers and nonresponders). Subjects were randomized in a 1:1 ratio and stratified by cirrhosis (presence vs. absence) and HCV genotype (2 vs. 3). There were 103 patients in the 12 week treatment group and 98 patients in the 16 week treatment group. The response was represented by SVR at 12

weeks, also known as SVR12. The overall SVR12 was 71% in the group treated for 16 weeks vs. 50% in the group treated for 12 weeks. For genotype 2, the SVR12 was 89% in the 16 week treatment group vs. 82% in the 12 week treatment group. For genotype 3, the SVR12 was 62% in the 16 week treatment group vs. 30% in the 12 week treatment group. There were no virologic failures in either group. The relapse rate was 11% in the 16 week treatment group vs. 18% in the 12 week treatment group in genotype 2 patients. In genotype 3 patients, the relapse rate was 38% in the 16 week treatment group vs. 66% in the 12 week treatment group. More data regarding a cirrhosis breakout and interferon classification is available in the package insert.

Treatment Naïve and Previously Treated Adults with Genotype 2 or 3
The VALENCE trial evaluated Sovaldi in combination with weight-based ribavirin for the treatment of genotype 2 or 3 HCV infection in treatment-naïve subjects or subjects who did not achieve SVR with prior interferon-based treatment, including subjects with compensated cirrhosis. The original trial design was a 4 to 1 randomization to Sovaldi + ribavirin for 12 weeks or placebo. Based on emerging data, this trial was unblinded and all genotype 2 HCV-infected subjects continued the original planned treatment and received Sovaldi + ribavirin for 12 weeks, and duration of treatment with Sovaldi + ribavirin in genotype 3 HCV-infected subjects was extended to 24 weeks. Eleven genotype 3 subjects had already completed Sovaldi + ribavirin for 12 weeks at the time of the amendment. The response was represented by SVR at 12 weeks, also known as SVR12. There were 73 patients in the 12 week treatment group (genotype 2) vs. 250 patients in the 24 week treatment group (genotype 3). The overall SVR12 was 93% in the 12 week genotype 2 group vs. 84% in the 24 week genotype 3 group. There were no virologic failures in the 12 week genotype 2 group and 1 in the 24 week genotype 3 group. The relapse rate was 14% in the 24 week genotype 3 group vs. 7% in the 12 week genotype 2 group.

Subjects Co-infected with HCV and HIV-1
Sovaldi was studied in an open-label clinical trial (Study PHOTON-1) evaluating the safety and efficacy of 12 or 24 weeks of treatment with Sovaldi and ribavirin in subjects with genotype 1, 2 or 3 CHC co-infected with HIV-1. Genotype 2 and 3 subjects were either HCV treatment-naïve or experienced, whereas genotype 1 subjects were all treatment-naïve. Subjects received 400 mg Sovaldi and weight-based ribavirin (1000 mg for subjects weighing < 75 kg or 1200 mg for subjects weighing ≥ 75kg) daily for 12 or 24 weeks based on genotype and prior treatment history. Subjects were either not on antiretroviral therapy with a CD4+ cell count > 500 cells/mm3 or had virologically suppressed HIV-1 with a CD4+ cell count > 200 cells/mm3. There were 114 patients with genotype

1, 26 patients with genotype 2, and 13 patients with genotype 3. The response was represented by SVR at 12 weeks, also known as SVR12. The overall SVR12 rates were as follows for genotypes 1, 2, and 3, respectively: 76%, 88%, and 92%. There was virologic failure in 1% of genotype 1 patients and 4% of genotype 2 patients. Twenty-two percent (22%) of patients with genotype 2 relapsed vs. none in the genotype 2 group vs. 8% in the genotype 3 group.

Pediatrics
The efficacy of Sovaldi in HCV-infected pediatric subjects 3 years of age and older was evaluated in 106 subjects with HCV genotype 2 (N = 31) or genotype 3 (N = 75) in a Phase 2, open label clinical trial. Subjects with HCV genotype 2 or 3 infection in the trial were treated with Sovaldi and weight-based ribavirin for 12 or 24 weeks, respectively.

Subjects 12 Years to <18 Years of Age: Sovaldi was evaluated in 52 subjects 12 years to <18 years of age with HCV genotype 2 (N = 13) or genotype 3 (N = 39) infection. The SVR12 rate was 100% [13/13] in genotype 2 subjects and 97% [38/39] in genotype 3 subjects. No subject experienced on-treatment virologic failure or relapse.

Subjects 6 Years to <12 Years of Age: Sovaldi was evaluated in 41 subjects 6 years to <12 years of age with HCV genotype 2 (N = 13) or genotype 3 (N = 28) infection. The SVR12 rate was 100% (13/13) in genotype 2 and 100% (28/28) in genotype 3 subjects.). No subjects experienced on-treatment virologic failure or relapse.
Subjects 3 Years to <6 Years of Age: Sovaldi was evaluated in 13 subjects 3 years to <6 years of age with HCV genotype 2 (N = 5) or genotype 3 (N = 8) infection. The SVR12 rate was 80% (4/5) in genotype 2 subjects and 100% (8/8) in genotype 3 subjects. No subjects experienced on-treatment virologic failure or relapse. One subject prematurely discontinued study treatment due to an adverse event.

References

1. Available at: www.cdc.gov/hepatitis/HCV/index.htm.
2. Sovaldi tablets [package insert]. Foster City, CA: Gilead Sciences, Inc.; Revised September 2019.
3. Recommendations for Testing, Managing, and Treating Hepatitis C. American Association for the Study of liver diseases. Updated January 2021.

Policy History

Original Effective Date: 01/15/2014
Current Effective Date: 11/13/2023

01/09/2014	Medical Policy Committee review
01/15/2014	Medical Policy Implementation Committee approval. New policy.
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval. Restricted use of Sovaldi to patients with F3/F4 or equivalent scenario listed in the patient selection criteria (high risk, extrahepatic manifestations, etc). Added criteria bullet requiring that the patient has NOT used a sofosbuvir containing regimen in the past (e.g. Sovaldi, Harvoni). Also will require Harvoni to be used in lieu of Sovaldi plus ribavirin for 24 weeks in those that are interferon ineligible.
02/05/2015	Medical Policy Committee review
02/18/2015	Medical Policy Implementation Committee approval. Removed any mention of F3/F4. Updated background info. Clarified that patient should NOT have decompensated cirrhosis.
12/03/2015	Medical Policy Committee review
12/16/2015	Medical Policy Implementation Committee approval. Added off label (guideline supported) indication for genotype 3 patients using 12 weeks of Sovaldi plus peg interferon plus ribavirin.
12/01/2016	Medical Policy Committee review
12/21/2016	Medical Policy Implementation Committee approval. No change to coverage.
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Changed from Harvoni first to Epclusa or Harvoni first for genotype interferon ineligible.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Updated policy with pediatrics information.
11/05/2020	Medical Policy Committee review

11/11/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. Removed the mention of the Daklinza Medical Policy inside of the policy.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 10/2024

*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 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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.