LOUISIANA BLUE

Pharmacotherapy for Primary Biliary Cholangitis

Policy # 00538
Original Effective Date: 11/16/2016
Current Effective Date: 12/09/2024

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.

obeticholic acid (Ocaliva®)

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 obeticholic acid (Ocaliva®)‡ for the treatment of primary biliary cholangitis (PBC) to be **eligible for coverage.****

Patient Selection Criteria

Initial Authorization (1 year):

Coverage eligibility for obeticholic acid (Ocaliva) will considered when the following criteria are met:

- Patient has a diagnosis of primary biliary cholangitis (PBC) confirmed by meeting at least TWO of the following criteria (a,b, and/or c):
    a. Alkaline phosphatase (ALP) elevated above the upper limit of normal as defined by normal laboratory reference values; AND/OR
    b. Positive anti-mitochondrial antibodies (AMAs) or other PBC-specific autoantibodies, including sp100 or gp210, if AMA is negative; AND/OR
    c. Histologic evidence of PBC from a liver biopsy; AND
- Patient does NOT have cirrhosis OR patient has compensated cirrhosis withOUT evidence of portal hypertension; AND
- Patient is 18 years of age or older; AND
- Patient meets ONE of the following (a or b):
    a. Patient is using Ocaliva in combination with ursodeoxycholic acid (URSO®‡, URSO Forte®, ursodiol)‡ due to an inadequate response to ursodeoxycholic acid (URSO, URSO Forte, ursodiol) AFTER 1 year of therapy with ursodeoxycholic acid (URSO, URSO Forte, ursodiol). Inadequate response is defined as meeting ONE of the following (i or ii):
        i. ALP greater than or equal to 1.67 times the upper limit of normal; OR

ii. Total bilirubin greater than the upper limit of normal but less than two times the upper limit of normal; OR

b. Patient is using Ocaliva as monotherapy due to an intolerance to ursodeoxycholic acid (URSO, URSO Forte, ursodiol); AND

- Requested drug will not be used in combination with seladelpar (Livdelzi®)‡ or elafibranor (Iqirvo®)‡.

Re-authorization (1 year)
Coverage eligibility for obeticholic acid (Ocaliva) will be considered when the following criteria are met:

- Patient has responded to Ocaliva therapy as determined by the prescribing physician (e.g., improved biochemical markers of primary biliary cholangitis [PBC] {e.g., alkaline phosphatase (ALP), bilirubin, gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT) levels}); AND
- Patient does NOT have cirrhosis OR patient has compensated cirrhosis withOUT evidence of portal hypertension; AND
- Requested drug will not be used in combination with seladelpar (Livdelzi) or elafibranor (Iqirvo).

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 obeticholic acid (Ocaliva) for any use other than its FDA approved indication OR when the patient selection criteria are not met to be **investigational.***

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Elafibranor (Iqirvo®) and seladelpar (Livdelzi®)

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 elafibranor (Iqirvo) or seladelpar (Livdelzi) for the treatment of primary biliary cholangitis (PBC) to be **eligible for coverage.****

Patient Selection Criteria

Initial Authorization:

Coverage eligibility for the requested drug will be considered when the following criteria are met:

- Patient has a diagnosis of primary biliary cholangitis (PBC) confirmed by meeting at least TWO of the following criteria (a, b and/or c):
    a. Alkaline phosphatase (ALP) elevated above the upper limit of normal as defined by normal laboratory reference values; AND/OR
    b. Positive anti-mitochondrial antibodies (AMAs), or other PBC-specific autoantibodies, including sp100 or gp210, if AMA is negative; AND/OR
    c. Histologic evidence of PBC from a liver biopsy; AND
- Patient does NOT have decompensated cirrhosis or have a history of a hepatic decompensation event (Note: Examples of hepatic decompensation include ascites, gastroesophageal varices, variceal bleeding, hepatic encephalopathy, and coagulopathy); AND
- Patient does NOT have complete biliary obstruction; AND
- Patient is 18 years of age or older; AND
- For Iqirvo requests: If the patient is a female of reproductive potential, provider attests that the patient is NOT currently pregnant and is willing to use effective contraception; AND
- Patient meets ONE of the following (a or b):
    a. Patient is using the requested medication in combination with ursodeoxycholic acid (URSO, URSO Forte, ursodiol) due to an inadequate response to ursodeoxycholic acid (URSO, URSO Forte, ursodiol) AFTER 1 year of therapy with ursodeoxycholic acid (URSO, URSO Forte, ursodiol). Inadequate response is defined as meeting ONE of the following (i or ii):
        i. ALP greater than or equal to 1.67 times the upper limit of normal; OR
        ii. Total bilirubin greater than the upper limit of normal but less than two times the upper limit of normal; OR
    b. Patient is using the requested drug as monotherapy due to an intolerance to ursodeoxycholic acid (URSO, URSO Forte, ursodiol); AND

- Patient will not use the requested drug in combination with obeticholic acid (Ocaliva) or another peroxisome proliferator-activated receptor (PPAR) agonist used for the treatment of PBC.

Re-authorization

- Patient has received an initial authorization for the requested medication; AND
- Patient will continue to use the requested medication in combination with ursodeoxycholic acid in the absence of any documented intolerance to ursodeoxycholic acid (URSO, URSO Forte, ursodiol); AND
- Patient has responded to therapy with the requested medication as determined by the prescribing physician (e.g., improved biochemical markers of primary biliary cholangitis [PBC] {e.g., alkaline phosphatase (ALP), bilirubin, gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT) levels}); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient does NOT have decompensated cirrhosis or have a history of a hepatic decompensation event. (Note: Examples of hepatic decompensation include ascites, gastroesophageal varices, variceal bleeding, hepatic encephalopathy, and coagulopathy); AND
- Patient does NOT have complete biliary obstruction; AND
- Patient will not use the requested drug in combination with obeticholic acid (Ocaliva) or another peroxisome proliferator-activated receptor (PPAR) agonist used for the treatment of PBC.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the continued use of elafibranor (Iqirvo) or seladelpar (Livdelzi) when the patient has not experienced improvement while on therapy 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 elafibranor (Iqirvo) or seladelpar (Livdelzi) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary**) to be **investigational.***

Background/Overview

Ocaliva is a farsenoid X receptor (FXR) agonist indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. The FDA approved Ocaliva under an accelerated approval based on a reduction in ALP. An improvement in survival or disease related symptoms has NOT been established. The FDA also states that continued approval for Ocaliva for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. In 2021, a boxed warning was added to Ocaliva. Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with Ocaliva treatment in PBC patients with cirrhosis, either compensated or decompensated. Among post-marketing cases reporting it, median time to hepatic decompensation (e.g., new onset ascites) was 4 months for patients with compensated cirrhosis; median time to a new decompensation event (e.g., hepatic encephalopathy) was 2.5 months for patients with decompensated cirrhosis. It is recommended to discontinue Ocaliva in patients who develop hepatic decompensation, who have compensated cirrhosis and portal hypertension, who experience clinically significant hepatic adverse reactions, or who develop complete biliary obstruction. Ocaliva is supplied as 5 mg and 10 mg tablets. The starting dose of Ocaliva is 5 mg once daily in adults who have not achieved an adequate response to an appropriate dosage of UDCA for at least 1 year or are intolerant to UDCA. If an adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months of Ocaliva 5 mg daily and the patient is tolerating the medication, the dosage of Ocaliva can be increased to 10 mg once daily (which is also the maximum dosage).

Iqirvo and Livdelzi, both peroxisome proliferator-activated receptor (PPAR) agonists, are indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. Although the mechanism by which Iqirvo and Livdelzi exert their therapeutic effect is not fully understood, it is thought to inhibit bile acid synthesis through activation of the peroxisome proliferator-activated receptors. Both drugs activate PPAR-delta, while Iqirvo is unique in that it also activates PPAR-alpha. The recommended dosage of Iqirvo is 80 mg orally once daily with or without food. The prescribing information for Iqirvo states that patients should be evaluated for muscle pain or myopathy prior to beginning treatment with Iqirvo. In addition, prescribers should verify that females of reproductive potential are not pregnant prior to treatment initiation. Effective contraception should also be used as Iqirvo may cause fetal harm. The recommended dose of Livdelzi is 10 mg taken orally once daily. The label for Livdelzi includes warnings involving fractures, liver test abnormalities, and biliary obstruction. The safety and efficacy of both Iqirvo and Livdelzi in patients with decompensated cirrhosis have not been established. Use of these drugs is not recommended in patients who have or develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy). Patients with cirrhosis should be closely monitored for evidence of decompensation.

Primary Biliary Cholangitis
Primary biliary cholangitis (previously referred to as primary biliary cirrhosis) is a rare liver disease characterized by an ongoing immunologic attack in the intralobular ducts. The exact cause of PBC is unknown, but it is presumed to be the result of a combination of both genetic and environmental factors leading to the autoimmune destruction of small and medium intrahepatic bile ducts. This immunologic attack eventually leads to cholestasis, which further progresses to fibrosis, cirrhosis and liver failure. In addition, a number of complications occur due to primary biliary cholangitis such as pruritis, metabolic bone disease, hypercholesterolemia and xanthomas, malabsorption, vitamin deficiencies, hypothyroidism and anemia. The goal of therapy in PBC is to prevent disease progression and manage symptoms and complications related to chronic cholestasis. Patients who do not respond to second-line treatments and progress to end-stage liver disease will require liver transplantation. There are currently four products that are FDA approved for the treatment of this condition. Ursodeoxycholic acid (URSO, URSO Forte, ursodiol) is used as first-line treatment of PBC. However, about 40% of patients have a suboptimal response to UDCA and some cannot tolerate UDCA, meaning many patients require second-line therapy. Second-line treatment options include obeticholic acid (Ocaliva), elafibranor (Iqirvo), and seladelpar (Livdelzi). Per their FDA approved labels, these options should only be considered in addition to UDCA for patients with an inadequate response to UDCA or as monotherapy for patients who cannot tolerate UDCA. While there have been no head-to-head comparisons of these products, each have varying degrees of safety concerns. Iqirvo has warnings regarding muscle symptoms (e.g., myalgia, myopathy), fractures, and adverse effects on fetal and newborn development. Ocaliva's label includes a Boxed Warning for hepatic decompensation and failure in patients with PBC and cirrhosis, and is contraindicated in patients with decompensated cirrhosis, a prior decompensation event, or compensated cirrhosis who have evidence of portal hypertension. In addition, Ocaliva can cause pruritus or worsen existing pruritus in many patients, which limits its use. It should be noted that Ocalvia, Iqirvo, and Livdelzi were approved under accelerated approval for the treatment of PBC and continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Ocaliva was approved in May of 2016 for the treatment of primary biliary cholangitis in combination with UDCA in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. In 2021, a boxed warning was added to Ocaliva. It states: "Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with Ocaliva treatment in primary biliary cholangitis patients with either compensated or decompensated cirrhosis. Ocaliva is contraindicated in primary biliary cholangitis patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension. Permanently discontinue Ocaliva in patients who develop laboratory or clinical evidence of hepatic decompensation, have compensated cirrhosis and develop evidence of portal hypertension, or experience clinically significant hepatic adverse reactions while on treatment."

Iqirvo and Livdelzi were both approved in 2024 for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA. This indication was approved under accelerated approval based on reduction of alkaline phosphatase (ALP). Improvement in survival or prevention of liver decompensation events have not been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

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.

Ocaliva

Ocaliva's safety and efficacy was evaluated in a randomized, double-blind, placebo-controlled, 12-month trial in 216 patients with primary biliary cholangitis who were taking ursodeoxycholic acid for at least 12 months or who were unable to tolerate ursodeoxycholic acid. Patients included in the trial had an alkaline phosphatase (ALP) of 1.67 times the upper limit or normal or greater and/or if the total bilirubin was greater than 1 times the upper limit of normal, but less than 2 times the upper limit of normal. Patients were randomized to receive either Ocaliva 10 mg once daily for the entire 12 months of the trial, Ocaliva titration (5 mg once daily for the initial 6 months, with the option to increase to 10 mg once daily for the last 6 months if the patient was tolerating Ocaliva but had ALP 1.67 times the upper limit of normal or greater and/or total bilirubin greater than the upper limit of normal, or less than 15% ALP reduction), or placebo. Ocaliva was administered with ursodeoxycholic acid in 93% of patients during the trial, while 7% were unable to tolerate the ursodeoxycholic acid. The primary endpoint was a responder analysis at month 12. The response included three criteria: ALP less than 1.67 times the upper limit of normal, total bilirubin less than or equal to the upper limit of normal, and an ALP decrease of at least 15%. The responder rate was 48% in the Ocaliva 10 mg group, 46% in the Ocaliva titration group, and 10% in the placebo group.

Iqirvo

The efficacy of Iqirvo was evaluated in one randomized, double-blind, placebo-controlled Phase III pivotal study which included 161 adults with PBC with an inadequate response or intolerance to UDCA. Patients were randomized to receive Iqirvo 80 mg or placebo once daily for at least 52 weeks. When applicable, patients continued their pre-study dose of UDCA throughout the study. Patients were included in the study if their ALP was greater than or equal to 1.67-times the upper limit of normal (ULN) and total bilirubin (TB) was less than or equal to 2-times the ULN. Patients were excluded if they had other liver disease or in case of decompensated cirrhosis. The primary endpoint was the proportion of patients achieving a biochemical response, which was achieved if a

patient met all of the following at week 52: an ALP level < 1.67 times the ULN with a ≥ 15% reduction in ALP, and a total bilirubin ≤ the ULN. Key secondary endpoints were normalization of the ALP level at week 52 and a change in pruritus intensity, assessed by the WI-NRS, from baseline through week 24 and week 52.

At week 52, 51% of patients receiving Iqirvo achieved a biochemical response compared with 4% of patients receiving placebo, resulting in a treatment difference of 47% (95% confidence interval [CI]: 32%, 57%) [P < 0.001]. A response to Iqirvo appeared to occur within 4 weeks after initiation of treatment and was maintained through week 52. Several preplanned subgroup analyses were conducted based on age, itch severity, disease severity, and baseline bilirubin and ALP levels. In all subgroups, the odds of achieving a biochemical response favored Iqirvo vs. placebo. In patients with moderate to severe pruritus, the least-squares mean change in the WI-NRS score was not significantly different between both groups from baseline through Week 52. However, the changes from baseline to week 52 appeared to favor Iqirvo over placebo for the itch domain of the PBC-40 quality-of-life questionnaire (least-squares mean difference -2.3; 95% CI: -4.0, -0.7) and for the total score on the 5-D itch scale (least-squares mean difference -3.0; 95% CI: -5.5, -0.5). Changes in other domains of the PBC-40 questionnaire over 52 weeks were similar between the two groups.

Livdelzi
The efficacy of Livdelzi was evaluated in one 12-month, randomized, double-blind, placebo-controlled trial. The study included 193 adult patients with PBC with an inadequate response or intolerance to UDCA. Patients were included in the trial if their ALP was greater than or equal to 1.67-times the ULN and total bilirubin (TB) was less than or equal to 2-times the ULN. Patients were excluded from the trial if they had other chronic liver diseases, clinically important hepatic decompensation including portal hypertension with complications, or cirrhosis with complications (e.g., Model for End Stage Liver Disease [MELD] score of 12 or greater, known esophageal varices or history of variceal bleeds, history of hepatorenal syndrome). Patients were randomized to receive Livdelzi 10 mg or placebo once daily for 12 months. Livdelzi or placebo was administered in combination with UDCA in 181 (94%) patients during the trial, or as a monotherapy in 12 (6%) patients who were unable to tolerate UDCA.

The primary endpoint was biochemical response at month 12, where biochemical response was defined as achieving ALP less than 1.67-times ULN, an ALP decrease of greater than or equal to 15% from baseline, and TB less than or equal to ULN. The ULN for ALP was defined as 116 U/L. The ULN for TB was defined as 1.1 mg/dL. Key secondary endpoints were normalization of the ALP level at month 12 and a change from baseline in the weekly mean pruritus score, assessed by the pruritus NRS, at month 6.

At month 12, a biochemical response was achieved in 61.7% of patients receiving Livdelzi compared with 20% of patients receiving placebo, resulting in a treatment difference of 41.7% (95% confidence interval [CI]: 27.7%, 53.4%) [P < 0.001]. A trend of lower ALP in the Livdelzi group compared with the placebo group was observed starting at month 1. Several preplanned subgroup

analyses were conducted based on age, pruritis severity, baseline ALP, presence of cirrhosis and concomitant treatment with UDCA. Although subgroup populations comprised small sample sizes, the odds of achieving a biochemical response favored Livdelzi vs. placebo. In patients with moderate to severe pruritus (baseline average pruritus score ≥ 4 [37% of patients {n = 72/193}]), the least-squares mean change in the pruritus NRS score at month 6 was -3.2 for Livdelzi compared with -1.7 with placebo. This resulted in a significant least-squares mean difference of -1.5 (95% CI: -2.5, -0.5 [P = 0.005]). This difference was maintained through month 12. Additionally, reduction in itch from baseline to month 12, as measured by the 5-D itch total score and in all individual domains except direction, appeared to be greater in patients who were treated with Livdelzi than in patients who received placebo.

Livdelzi is the only agent amongst the three to demonstrate a clinically meaningful reduction in pruritus in its pivotal trial.

References

1. Ocaliva [package insert]. Intercept Pharmaceuticals, Inc. New York, New York. May 2021.
2. UpToDate. Primary Biliary Cholangitis. Accessed October 2016.
3. Iqirvo [package insert]. Ipsen Biopharmaceuticals, Inc. Cambridge, MA. June 2024.
4. Iqirvo Drug Evaluation. Express Scripts. June 2024.
5. Iqirvo (elafibranor) New Drug Review. IPD Anaylytics. July 2024.
6. Livdelzi [package insert]. Gilead Sciences, Inc. Foster City, CA. August 2024.
7. Livdelzi Drug Evaluation. Express Scripts. August 2024.

Policy History

Original Effective Date: 11/16/2016
Current Effective Date: 12/09/2024

11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. New policy.
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. No change to coverage.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. No change to coverage.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. No change to coverage.
11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. No change to coverage.
11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. Added a criterion to note that patients should either have no cirrhosis OR compensated cirrhosis withOUT evidence of portal hypertension due to a new boxed warning for Ocaliva.

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11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. No change to coverage.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/07/2024	Medical Policy Committee review
11/13/2024	Medical Policy Implementation Committee approval. Title changed from "obeticholic acid (Ocaliva®)" to "Pharmacotherapy for Primary Biliary Cholangitis." Added new drugs, Iqirvo and Livdelzi, to the policy with relevant criteria and background information.

Next Scheduled Review Date: 11/2025

*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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.