

maralixibat (Livmarli™)

Policy # 00775

Original Effective Date: 03/14/2022

Current Effective Date: 08/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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.*

Alagille Syndrome

Based on review of available data, the Company may consider maralixibat (Livmarli)™† for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for maralixibat (Livmarli) for the treatment of cholestatic pruritus in patients with Alagille syndrome will be considered when the following criteria are met:

Initial:

- Patient has a diagnosis of cholestatic pruritus due to Alagille syndrome (ALGS); AND
- Alagille syndrome diagnosis has been confirmed by one of the following:
 - Genetic testing demonstrating *JAG1* or *NOTCH2* deletion or mutations; OR
 - Liver biopsy demonstrating bile duct paucity consistent with ALGS; OR
 - Presence of three or more major clinical features of ALGS as listed below:
 - Hepatic abnormality (e.g., cholestasis)
 - Cardiac abnormality (e.g., stenosis of the peripheral pulmonary artery and its branches)
 - Skeletal abnormality (e.g., butterfly vertebrae)
 - Ocular abnormality (e.g., posterior embryotoxon)
 - Characteristic facial features (e.g., triangular-shaped face with a broad forehead and a pointed chin, bulbous tip of the nose, deeply set eyes, and hypertelorism);
 - Vascular abnormalities (e.g., intracranial bleeds, systemic vascular anomalies)
 - Renal structural or functional abnormality (e.g., abnormally small size, cysts); AND

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(Note: Although most patients with ALGS have an identifiable pathogenic variant in JAG1 or NOTCH2, a small subset of clinically diagnosed patients do not have a detectable causative variant. Therefore, absence of a pathogenic variant does not exclude the diagnosis when clinical and/or histopathologic findings are strongly supportive of ALGS.)

- Patient is at least 3 months of age or older; AND
- Patient's serum bile acid concentration is above the upper limit of normal reference range for the reporting laboratory; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met).*

- Patient does NOT have cirrhosis; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met).*
- Patient does NOT have portal hypertension; AND
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met).*
- Patient does NOT have a history of a hepatic decompensation event (examples include variceal hemorrhage, ascites, hepatic encephalopathy); AND
- Requested formulation is Livmarli 9.5 mg/mL oral solution or Livmarli tablets; AND
- Dose of the requested medication will NOT exceed 28.5 mg per day; AND
- Dose of the requested medication will NOT exceed 380 micrograms per kilogram per day; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) TWO other medications for this condition (e.g., cholestyramine, rifampin, and ursodiol) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient.
*(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 will not use Livmarli in combination with odeixibat (BylvayTM)[‡].

Continuation:

- Initial patient selection criteria were met; AND
- Patient does NOT have cirrhosis; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met).*
- Patient does NOT have portal hypertension; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met).*
- Patient does NOT have a history of a hepatic decompensation event (examples include variceal hemorrhage, ascites, hepatic encephalopathy); AND
- Requested formulation is Livmarli 9.5 mg/mL oral solution or Livmarli tablets; AND
- Dose of the requested medication will NOT exceed 28.5 mg per day; AND

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- Dose of the requested medication will NOT exceed 380 micrograms per kilogram per day; AND
- Patient has responded to therapy with the requested product (i.e., a decrease in serum bile acids and a decrease in pruritis); 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 will not use Livmarli in combination with odevixibat (Bylvay).

Progressive Familial Intrahepatic Cholestasis

Based on review of available data, the Company may consider maralixibat (Livmarli) for the treatment of cholestatic pruritus in patients with progressive familial intrahepatic cholestasis (PFIC) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for maralixibat (Livmarli) for the treatment of cholestatic pruritus in patients with progressive familial intrahepatic cholestasis will be considered when the following criteria are met:

Initial:

- Patient has a diagnosis of pruritus due to progressive familial intrahepatic cholestasis (PFIC) Types 1, 2, 3, 4 or 6; AND
*(Note: This specific patient selection criterion is partially an additional Company requirement for coverage eligibility. Requests for Type 5 PFIC will be denied as not medically necessary** if not met).*
- Patient meets **one** of the following, which confirms the diagnosis of PFIC:
 - Type 1: Presence of mutations in the *ATP8B1* gene; OR
 - Type 2: Presence of mutations in the *ABCB11* gene; OR
 - Type 3: Presence of mutations in the *ABCB4* gene; OR
 - Type 4: Presence of mutations in the tight junction protein 2 gene (*TJP2*); OR
 - Type 6: Presence of mutations in the myosin 5B gene (*MYO5B*); AND
- Patient has the presence of moderate to severe pruritus (per the prescriber); AND
*(Note: This specific patient selection criterion is partially an additional Company requirement for coverage eligibility. Requests for pruritus severity that are not considered moderate to severe will be denied as not medically necessary** if not met).*
- Patient is 12 months of age or older; AND
- Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory; 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 a pathologic variant of the *ABCB11* gene that predicts non-function or complete absence of bile salt export pump protein (BSEP-3); AND
- Patient does NOT have cirrhosis; 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 portal hypertension; AND

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*(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 a history of a hepatic decompensation event (examples include variceal hemorrhage, ascites, hepatic encephalopathy); AND
- Patient has NOT had a liver transplant; 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).*

- Requested formulation is Livmarli 19 mg/mL oral solution or Livmarli tablets; AND
- Dose of the requested medication will NOT exceed 38 mg per day; AND
- Dose of the requested medication will NOT exceed 570 micrograms per kilogram per dose; AND

- Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC ursodeoxycholic acid unless there is clinical evidence or patient history that suggests the use of this product will be ineffective or cause an adverse reaction to the patient; 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 has tried and failed (e.g., intolerance or inadequate response) ONE of the following: GENERIC rifampin, GENERIC naltrexone, or GENERIC sertraline, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; 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 will not use Livmarli in combination with odeixibat (Bylvay).

Continuation:

- Patient has received an initial authorization for Livmarli; AND

- Patient does NOT have cirrhosis; 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 portal hypertension; 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 a history of a hepatic decompensation event (examples include variceal hemorrhage, ascites, hepatic encephalopathy); AND

- Patient has NOT had a liver transplant; 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).*

- Requested formulation is Livmarli 19 mg/mL oral solution or Livmarli tablets; AND

- Dose of the requested medication will NOT exceed 38 mg per day; AND

- Dose of the requested medication will NOT exceed 570 micrograms per kilogram per dose; AND

- Patient has responded to therapy with the requested medication (e.g., decreased pruritus and/or decrease in serum bile acids); 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 will not use Livmarli in combination with odeixibat (Bylvay).

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of maralixibat (Livmarli) when the patient has cirrhosis or portal hypertension to be **not medically necessary**.**

Based on review of available data, the Company considers the use of maralixibat (Livmarli) when the patient does NOT have a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory to be **not medically necessary**.**

Based on review of available data, the Company considers the use of maralixibat (Livmarli) when the patient has not tried and failed (e.g., intolerance or inadequate response) other required medications for the requested condition to be **not medically necessary**.**

Based on review of available data, the Company considers the use of maralixibat (Livmarli) when the patient has Type 5 progressive familial intrahepatic cholestasis (PFIC) to be **not medically necessary**.**

Based on review of available data, the Company considers the use of maralixibat (Livmarli) when the patient does NOT have pruritus that is considered to be moderate to severe to be **not medically necessary**.**

Based on review of available data, the Company considers the use of maralixibat (Livmarli) when the patient has had a liver transplant to be **not medically necessary**.**

Based on review of available data, the Company considers the continued use of maralixibat (Livmarli) when the patient has not responded to 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 maralixibat (Livmarli) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational**.*

Background/Overview

Livmarli is an ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 3 months of age and older and for the treatment of cholestatic pruritus in patients with progressive familial intrahepatic cholestasis (PFIC) 12 months of age and older. Livmarli is supplied as an oral solution in concentrations containing 9.5 mg or 19 mg of drug per milliliter of solution and as tablets. The two strengths of Livmarli oral solution should not be substituted for one another. Special attention should be given to the accurate calculation of the dose volume of Livmarli. This is especially important for pediatric patients less than 5 years old as Livmarli oral solution contains the excipient propylene glycol. In ALGS, the 9.5mg/mL concentration or tablets should be used for treatment. The recommended dosage is 380 mcg/kg once

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daily, taken 30 minutes before the first meal of the day. Dosing should be started at 190 mcg/kg administered orally once daily; after one week, the dosage can be increased to 380 mcg/kg once daily, as tolerated. The maximum daily dose volume for patients above 70kg is 3 mL or 28.5 mg per day. In PFIC, the 19mg/mL concentration or tablets should be used. The recommended dosage for patients with PFIC is 570 mcg/kg twice daily 30 minutes before a meal. The starting dose is 285 mcg/kg once daily in the morning and should be increased to 285 mcg/kg twice daily, 428 mcg/kg twice daily, and then to 570 mcg/kg twice daily, as tolerated. The maximum daily dose should not exceed 38mg (4mL) per day. Refer to the package insert for complete details on dosing. The efficacy and safety of Livmarli in patients with clinically significant portal hypertension and in patients with decompensated cirrhosis have not been established. Livmarli is contraindicated in patients with prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

Alagille Syndrome (ALGS)

Alagille syndrome is an autosomal dominant liver disease which affects the bile acid transporters leading to chronic cholestasis and elevations of serum bile acids. This condition is primarily identified by the presence of a mutation or deletion of the *JAG1* gene or *NOTCH2* gene. Approximately 90% to 94% of patients with ALGS have identifiable pathogenic variants or deletions involving *JAG1*, while approximately 1% to 3% have pathogenic *NOTCH2* variants. A small proportion of patients with a clinical phenotype consistent with ALGS do not have an identifiable pathogenic variant despite comprehensive genetic testing.

Historically, the diagnosis of ALGS was based on the presence of bile duct paucity on liver biopsy in combination with characteristic clinical features. Classic diagnostic criteria included bile duct paucity plus at least three of five major clinical features: cholestatic liver disease, cardiac abnormalities, skeletal abnormalities, ocular abnormalities, and characteristic facial features. More recent guidance places greater emphasis on molecular confirmation, recognizing that a diagnosis of ALGS may be established by identification of a pathogenic *JAG1* or *NOTCH2* variant, even in the absence of the full spectrum of classic clinical manifestations. Conversely, patients without genetic confirmation may still be diagnosed based on characteristic clinical and histopathologic findings, including bile duct paucity and multisystem involvement consistent with ALGS.

Clinical manifestations commonly include cholestasis, pruritus, xanthomas, and jaundice. Additional organ involvement may affect the heart, skeleton, eyes, kidneys, and vasculature. The disorder exhibits variable expressivity and incomplete penetrance, resulting in a broad spectrum of disease severity. Progression of the disease can lead to fibrosis, cirrhosis, and in some cases, liver transplantation.

Livmarli decreases the reabsorption of bile acids from the terminal ileum. Although the exact mechanism by which Livmarli improves pruritus is not fully understood, its therapeutic effect is believed to be related to reduction of bile acid accumulation associated with cholestatic liver disease. Prior to the availability of IBAT inhibitors, off-label therapies such as ursodiol, rifampin, and cholestyramine were routinely used for symptomatic management of cholestatic pruritus and remain part of clinical practice. Ursodiol has demonstrated the ability to decrease the advancement of liver

fibrosis in related cholestatic conditions. Given the historical clinical use and acceptance of ursodiol, rifampin, and cholestyramine for cholestatic pruritus and Livmarli's primary outcome measurement of itch scores (and not outcomes data), it is reasonably appropriate to recommend a trial of off-label, yet clinically accepted, alternative medications.

Progressive Familial Intrahepatic Cholestasis (PFIC)

PFIC is a group of rare, genetic disorders characterized by impaired bile formation and bile acid transport, resulting in cholestasis and progressive liver disease. There are currently 6 types of PFIC: Types 1, 2, 3, 4, 5 and 6. An in-depth analysis of each type is beyond the scope of this medical policy. Livmarli clinical studies included Types 1, 2, 3, 4, and 6 PFIC. These types of PFIC are caused by mutations in the *ATP8B1*, *ABCB11*, *ABCB4*, *TJP2*, and *MYO5B* genes, respectively. As a result of the mutations, retention of bile acids occurs within the body. Bile flow is integral for the digestion and absorption of dietary fats, vitamins, and other nutrients. Bile flow also facilitates the elimination of excess cholesterol, bilirubin, waste, and toxins from the body. Due to the retention of bile acids in the body, common clinical manifestations include cholestasis, pruritus, jaundice, growth impairment, and nutritional deficiencies. Progressive disease may lead to fibrosis, cirrhosis, liver failure, and the need for liver transplantation.

Management of PFIC typically begins with nutritional optimization, including high-calorie diets, medium-chain triglyceride supplementation, and replacement of fat-soluble vitamins. Pharmacologic therapy is generally initiated to reduce cholestasis and improve symptoms, particularly pruritus. Ursodeoxycholic acid (UDCA) remains the most commonly used first-line pharmacologic treatment across PFIC subtypes. UDCA alters bile acid composition, increases bile flow, reduces the concentration of potentially toxic bile acids, and may provide additional hepatoprotective effects. These actions may improve cholestasis, reduce pruritus, and decrease the risk of bile-related complications.

Additional off-label therapies commonly used for management of cholestatic pruritus include cholestyramine, rifampin, naltrexone, and sertraline. A small study of patients with PFIC using ursodeoxycholic acid demonstrated improvements in liver function, hepatosplenomegaly, and pruritus for the majority of the group. European guidelines even discuss the use of ursodeoxycholic acid in this group of conditions. If pruritus is not relieved by ursodeoxycholic acid, then cholestyramine can be used to deplete the bile acid pool. Rifampin works by increasing the metabolism and excretion of pruritogens. Studies suggest that sertraline and naltrexone are also viable options for therapy in these patients. While cholestyramine has historically been used as a second-line option after UDCA, its effectiveness may be limited in PFIC due to reduced biliary bile acid excretion, and its use may be complicated by gastrointestinal adverse effects and drug-drug interactions. After the exhaustion of pharmacologic agents, surgical procedures to interrupt the circulation of bile acids are often successful.

In addition to Livmarli, a second ileal bile acid transporter (IBAT) inhibitor, odeixibat (Bylvay), has been approved by the Food and Drug Administration (FDA) for the treatment of these conditions. There have been no head-to-head studies comparing these two products to suggest clinical superiority; however, differences in acquisition costs and overall treatment expense may be important considerations when evaluating therapy selection.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Livmarli, approved in late 2021, is an ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older. In March of 2023, the FDA label was updated to include approval for patients 3 months of age and older. In March of 2024, Livmarli was approved for the treatment of cholestatic pruritus in patients 5 years of age and older with progressive familial intrahepatic cholestasis. In July 2024, the approval for the treatment of cholestatic pruritus in patients with progressive familial intrahepatic cholestasis was expanded to include patients 12 months of age and older.

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 regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Livmarli in ALGS was assessed in Trial 1, which consisted of an 18-week open-label treatment period; a 4-week randomized, double-blind, placebo-controlled drug-withdrawal period; a subsequent 26-week open-label treatment period; and a long-term open-label extension period.

Thirty-one pediatric Alagille syndrome patients with cholestasis and pruritus were enrolled, with 90.3% of patients receiving at least one medication to treat pruritus at study entry. All patients had a *JAG1* mutation. Patients were administered open-label treatment with Livmarli 380 mcg/kg once daily for 13 weeks after an initial 5-week dose-escalation period; two patients discontinued treatment during this first 18 weeks of open-label treatment. The 29 patients who completed the open-label treatment phase were then randomized to continue treatment with Livmarli or receive matching placebo during the 4-week drug withdrawal period at Weeks 19-22 (n = 16 placebo, n = 13 Livmarli). All 29 patients completed the randomized, blinded drug withdrawal period; subsequently, patients received open-label Livmarli at 380 mcg/kg once daily for an additional 26 weeks.

Given the patients' young age, a single-item observer-reported outcome was used to measure patients' pruritus symptoms as observed by their caregiver twice daily (once in the morning and once in the evening) on the Itch Reported Outcome Instrument (ItchRO[Obs]). Pruritus symptoms were assessed on a 5-point ordinal response scale, with scores ranging from 0 (none observed or reported) to 4 (very severe). Patients were included in Trial 1 if their average pruritus score was greater than 2.0 (moderate) in the 2 weeks prior to baseline. The average of the worst daily ItchRO(Obs) pruritus scores was computed for each week. For randomized patients, the mean (SD) at baseline (pre-treatment) was 3.1 (0.5) and the mean (SD) at Week 18 (pre-randomized withdrawal period) was 1.4 (0.9). On average, patients administered Livmarli for 22 weeks maintained pruritus reduction whereas those in the placebo group who were withdrawn from Livmarli after Week 18 returned to baseline pruritus scores by Week 22. After re-entering the open-label treatment phase,

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both randomized treatment groups had similar mean pruritus scores by Week 28, the first week placebo patients received the full dosage of Livmarli after withdrawal. These observer-rated pruritus results are supported by similar results on patient-rated pruritus in patients 5 years of age and older who were able to self-report their itching severity.

The efficacy of Livmarli in PFIC was evaluated in one 26-week, randomized, placebo-controlled pivotal trial. Efficacy was evaluated in 64 patients with a clinical genetic confirmation of PFIC. Patients had to have an elevated serum bile acid concentration along with presence of moderate to severe pruritus at baseline. Patients were randomized to receive Livmarli orally 570 mcg/kg (n = 33) or placebo (n = 31) twice daily. Most patients were on stable ursodeoxycholic acid (89.1%) or rifampicin (51.6%) therapy at baseline.

The same 5-point ordinal scratching scale used in Trial 1 was also used in Trial 2. Scratching scores were observed and reported by the patients' caregiver twice daily (once in the morning and once in the evening). Patients treated with Livmarli demonstrated greater improvement in pruritus compared with placebo.

References

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02/03/2022	Medical Policy Committee review
02/09/2022	Medical Policy Implementation Committee approval. New policy.
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. Updated criteria to reflect newest FDA label update for approval in patients 3 months of age and older.
07/02/2024	Medical Policy Committee review
07/10/2024	Medical Policy Implementation Committee approval. Added a new FDA approved indication PFIC, included relevant criteria and background information. Updated ALGS criteria to clarify that doses above the labeled maximum dose are not covered. Updated denial reasoning for ALGS criterion regarding the history of hepatic decompensation to investigational and criterion requiring serum bile acid concentrations above the upper limit of normal to not medically necessary.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Updated the age requirement for the treatment of cholestatic pruritus in patients with PFIC to include patients 12 months of age and older per the updated FDA package insert. Added new strength, 19 mg/mL solution, with relevant dosing criteria and background information.
08/07/2025	Medical Policy Committee review
08/13/2025	Medical Policy Implementation Committee approval. Added new formulation, Livmarli tablets, to the policy with relevant criteria and background information. Title changed from “maralixibat oral solution (Livmarli)” to “maralixibat (Livmarli)”.
07/21/2026	Pre Pharmacy & Therapeutics Committee review
07/22/2026	Pharmacy & Therapeutics Committee review approval. Updated ALGS diagnostic criteria to allow additional methods of diagnosis, including liver biopsy demonstrating bile duct paucity consistent with ALGS OR the presence of three or more major clinical features of ALGS as listed. Criteria for PFIC were updated to remove requirement of trial and failure of cholestyramine or colestipol. Requirement to try and fail odevoxibat (Bylvay) was also removed. Background information was updated to include recent published guidance.

Next Scheduled Review Date: 07/2027

*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

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- 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.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period.

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Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.