09-J4000-10

Original Effective Date: 01/01/22

Reviewed: 09/13/23

Revised: 06/15/24

Subject: Maralixibat (Livmarli®) Oral Solution

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Maralixibat (Livmarli) in an oral solution first approved by the U.S. Food and Drug Administration (FDA) in September 2021 for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older. In March 2023, this indication was expanded to include patients 3 months of age and older based on an open-label, multicenter study which showed a similar safety, tolerability, and pharmacokinetic profile to patients with ALGS >12 months of age. In March 2024, a new indication was FDA approved for the treatment of cholestatic pruritus in patients 5 years of age and older with progressive familial intrahepatic cholestasis (PFIC). Maralixibat is a non-systemic, reversible inhibitor of the ileal bile acid transporter (IBAT) that decreases the reabsorption of bile acids (primarily the salt forms) from the terminal ileum. It is the second IBAT inhibitor to be approved; the first being odevixibat (Bylvay).

Alagille syndrome is a rare, autosomal dominant genetic disorder that can affect multiple organ systems, including the liver, heart, skeleton, eyes, and kidneys. Most patients have mutations in one copy of the *JAG1* gene, but a small percentage (2%) have mutations of the *NOTCH2* gene. The estimated incidence of ALGS is approximately 1/30,000 to 1/45,000. The specific symptoms and severity of ALGS can vary greatly from one person to another. Approximately 90% of individuals with ALGS have a reduced number of bile ducts (bile duct paucity) that can progress to liver disease. Patients may present in the first 3 months of life with cholestasis, jaundice, poor weight gain and growth, and pruritus. Many individuals with ALGS also have heart abnormalities that can range from benign heart murmurs to serious structural defects. Individuals usually have distinctive facial features including deeply set and widely spaced (hypertelorism) eyes, a pointed chin, and broad forehead. One of the more problematic manifestations of ALGS is pruritus, which can lead to physical abrasions and scarring, as well as functional impacts (e.g., sleep and mood disorders) and deterioration in quality of life.

Progressive familial intrahepatic cholestasis (PFIC) is an ultra-rare, heterogeneous group of liver disorders of autosomal recessive inheritance that disrupt bile formation and are characterized by an early onset of cholestasis with pruritus and malabsorption, which rapidly progresses, eventually leading to liver failure. Most patients with PFIC require biliary diversion surgery or liver transplant by 30 years of age or earlier. The suspected incidence of PFIC is between 1 in 50,000 and 1 in 100,000 births and an estimated 600 children in the United States are afflicted. While PFIC types 1, 2, and 3 are the most common, new subtypes are still being discovered. Each subtype is uniquely categorized based on the mutated gene and resultant protein deficiency. For example, PFIC1 is due to a mutation in the ATP8B1 gene that encodes the FIC1 (familial intrahepatic cholestasis 1) protein, and PFIC2 is due to a mutation in the ABCB11 gene that encodes the BSEP (bile salt export pump). Each subtype has a unique clinical presentation, management strategies, and outcomes. Initial care for patients with PFIC addresses nutritional problems, including supplementation with and monitoring of fat-soluble vitamins. However, the most prominent and problematic manifestation of PFIC (in particular in types 1 and 2) is pruritis, which can lead to physical abrasions and scarring, as well as functional impacts (e.g., sleep and mood disorders) and deterioration in overall quality of life. Therapy-refractory persistent pruritus can be an indication for liver transplantation, even in the absence of liver failure. Liver transplantation is generally curative for patients with PFIC 1 and 2; however, patients with PFIC1 may have ongoing disease due to the extrahepatic expression of the FIC1 protein.

Maralixibat is the first pharmacologic therapy specifically approved for ALGS. Treatment previously relied on supportive pharmacologic therapy for symptomatic relief (e.g., ursodiol, rifampicin, cholestyramine, antihistamines) or surgical intervention (e.g., surgical biliary diversion, liver transplantation). According to the European Association for the Study of the Liver (EASL) guidelines, ursodiol is often a first-line medication for cholestasis although it's effect on pruritus varies, and the guidelines note that for ALGS specifically no effective medical treatment is known (prior to maralixibat). Rifampicin counteracts pruritus by increasing the metabolism of pruritogenic substances, prompting their renal elimination in hydroxylated forms. In addition, the antibacterial effect of rifampicin in the intestine may potentially modify the intestinal metabolism of pruritogenic substances. Because this treatment is well tolerated, and its efficacy has been demonstrated, rifampicin is widely considered a first-line treatment for cholestatic pruritus in children. The anion exchange resin cholestyramine was initially the only approved medication for cholestatic pruritus; however, its inconsistent efficacy and poor tolerance (nausea, constipation, diarrhea) often limits its use in children.

The safety and efficacy of maralixibat leading to FDA approval for Alagille syndrome was evaluated in the Phase 2 ICONIC study (NCT02160782, Trial 1 in the product labeling), 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 JAGGED1 mutation. Patients were administered open-label treatment with maralixibat 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 maralixibat or receive matching placebo during the 4-week drug withdrawal period at Weeks 19 to 22 (n=16 placebo, n=13 maralixibat). All 29 patients completed the randomized, blinded drug withdrawal period; subsequently, patients

received open label maralixibat at 380 mcg/kg once daily for an additional 26 weeks. Randomized patients had a median age of 5 years (range: 1 to 15 years) and 66% were male. The baseline mean (standard deviation) of liver test parameters were as follows: serum bile acid levels 280 (213) mcmol/L, AST 158 (68) units/L, and ALT 179 (112) units/L. 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 only included if their average pruritus score was greater than 2 (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 maralixibat for 22 weeks maintained pruritus reduction whereas those in the placebo group who were withdrawn from maralixibat after Week 18 returned to baseline pruritus scores by Week 22. Results from the placebo-controlled period are presented in the Table. After re-entering the open-label treatment phase, both randomized treatment groups had similar mean pruritus scores by Week 28, the first week placebo patients received the full dosage of maralixibat 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.

	Maralixibat (n=13)	**Placebo (n=16)**	**Mean Difference**
Week 22, Mean (95% CI)	1.6 (1.1, 2.1)	3.0 (2.6, 3.5	
Change from Week 18 to Week 22, Mean (95% CI)	0.2 (-0.3, 0.7)	1.6 (1.2, 2.1)	-1.4 (-2.1, -0.8)

Maralixibat is the second pharmacologic therapy specifically approved for PFIC. The first being another IBAT, odevixibat (Bylvay), in July 2021. Before IBAT therapy, treatment relied on supportive pharmacologic therapy for symptomatic relief (e.g., ursodiol, rifampicin, cholestyramine, antihistamines) or surgical intervention (e.g., surgical biliary diversion, liver transplantation). According to the European Association for the Study of the Liver (EASL) guidelines, ursodiol is the first line medication for cholestasis although it’s effect on pruritus varies. Ursodiol has been reported to improve biochemical tests in almost 50% of patients with PFIC3, but often does not affect PFIC1 and PFIC2. Rifampicin counteracts pruritus by increasing the metabolism of pruritogenic substances, prompting their renal elimination in hydroxylated forms. In addition, the antibacterial effect of rifampicin in the intestine may potentially modify the intestinal metabolism of pruritogenic substances. Because this treatment is well tolerated, and its efficacy has been demonstrated, rifampicin is widely considered a first-line treatment for cholestatic pruritus in children. The anion exchange resin cholestyramine was initially the only approved medication for cholestatic pruritus; however, its inconsistent efficacy and poor tolerance (nausea, constipation, diarrhea) often limits its use in children.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of maralixibat (Livmarli) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "11"):

1. Member has a confirmed diagnosis of **EITHER** of the following ("a" or "b"):
    a. Progressive familial intrahepatic cholestasis (PFIC) as evidenced by **BOTH** of the following ("i" and "ii"):
        i. Genetic testing demonstrating a gene mutation affiliated with progressive familial intrahepatic cholestasis (for example, mutations in *ATP8B1, ABCB11, ABCB4, TJP2, NR1H4, or Myo5b* genes) – *medical record documentation of the member's genetic testing results must be submitted*
        ii. A pretreatment (baseline) total serum bile acid concentration above the upper limit of normal (ULN) for the member's age [according to the reporting laboratory] - *medical record documentation of the member's baseline total serum bile acid level must be submitted*
    b. Alagille syndrome (ALGS) with cholestasis as evidenced by **BOTH** of the following ("i" and "ii"):
        i. Genetic testing demonstrating a mutation in the *JAG1* or *NOTCH2* genes* – *medical record documentation of the member's genetic testing results must be submitted*

        **Very rarely a patient may have ALGS with no identifiable gene mutation. In these cases, the specialist physician must provide medical record documentation detailing how the member's clinical work-up, signs and symptoms of disease, and differential diagnosis (i.e., exclusion of other causes) has confirmed the member has ALGS.*

        ii. Evidence of cholestasis as defined by **ANY** of the following ("1" to "4") - *medical records documenting at least one of the following must be submitted:*
            1. Pretreatment (baseline) total serum bile acid level greater than 3-times upper limit of normal (ULN) for the member's age [according to the reporting laboratory]
            2. Pretreatment (baseline) conjugated bilirubin greater than 1 mg/Dl
            3. Fat-soluble vitamin deficiency otherwise unexplainable
            4. Pretreatment (baseline) gamma-glutamyl transferase (GGT) greater than 3-times ULN for the member's age [according to the reporting laboratory].
2. Member does **NOT** have a diagnosis of PFIC2 with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3)
3. Member has a history of moderate-to-severe pruritus due to cholestasis associated with ALGS or PFIC - *medical records documenting the member's severity of pruritis and scratching must be submitted*
4. Member has **NOT** previously received a liver transplant
5. Member does **NOT** have clinical evidence of decompensated cirrhosis

6. **ANY** of the following regarding ursodiol treatment ("a", "b", or "c"):
    a. Member is currently being treated with ursodiol
    b. Member has had a previous trial of ursodiol treatment with minimal clinical benefit
    c. Member had intolerable adverse effects with or has a contraindication to treatment with ursodiol - *the specific intolerance or contraindication must be provided*.
7. Member has tried and had an inadequate response to at least **ONE** other systemic cholestasis pruritus treatment [cholestyramine or rifampin], **OR** the member has intolerances and/or contraindications to **BOTH** of these medications – *if applicable the specific intolerances and/or contraindications must be provided*
8. Maralixibat will **NOT** be used in combination with another ileal bile acid transporter (IBAT) inhibitor [for example, odevixibat (Bylvay)]
9. Maralixibat is prescribed by, or in consultation with, a gastroenterologist, hepatologist, or other physician who specializes in the management of ALGS or PFIC
10. Member is at least 3 months of age or older for the treatment of ALGS or 5 years or older for the treatment of PFIC
11. Dosage of maralixibat does not exceed the following based on the diagnosis:
    - ALGS – 380 mcg/kg body weight once daily (up to a maximum of 28.5 mg (3 mL) per day) [maximum of three 30 mL bottles per 30 days]
    - PFIC - 570 mcg/kg body weight twice daily (up to a maximum of 38 mg (4 mL) per day) [maximum of four 30 mL bottles per 30 days]

Approval duration: 6 months

Continuation of maralixibat (Livmarli) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "7"):

1. An authorization or reauthorization for maralixibat has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of ALGS or PFIC (if another health plan, documentation of a health plan-paid claim for maralixibat during the 90 days immediately before the authorization request must be submitted); **OR** the member has previously met **ALL** indication-specific criteria
2. Member has had a beneficial response to therapy as determined by a clinically meaningful reduction in pruritis – *medical record documentation citing the impact of treatment on the member's pruritis must be submitted*
3. Member has **NOT** received a liver transplant
4. Member does **NOT** have clinical evidence of decompensated cirrhosis
5. Maralixibat will **NOT** be used in combination with another ileal bile acid transporter (IBAT) inhibitor [for example, odevixibat (Bylvay)]
6. Maralixibat is prescribed by, or in consultation with, a gastroenterologist, hepatologist, or other physician who specializes in the management of ALGS or PFIC
7. Dosage of maralixibat does not exceed the following based on the diagnosis:

- ALGs – 380 mcg/kg body weight once daily (up to a maximum of 28.5 mg (3 mL) per day) [maximum of three 30 mL bottles per 30 days]
- PFIC - 570 mcg/kg body weight twice daily (up to a maximum of 38 mg (4 mL) per day) [maximum of four 30 mL bottles per 30 days]

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 3 months of age and older
  - The recommended dosage is 380 mcg/kg once daily, taken 30 minutes before the first meal of the day. Start dosing at 190 mcg/kg administered orally once daily; after one week, increase to 380 mcg/kg once daily, as tolerated. The maximum daily dose volume for patients above 70 kg is 3 mL or 28.5 mg per day. Refer to the product labeling Table 1: Volume per Dose (mL) by Patient Weight.
- Indicated for the treatment of cholestatic pruritus in patients 5 years of age and older with progressive familial intrahepatic cholestasis (PFIC). Limitations of Use: Livmarli is not recommended in a subgroup of PFIC type 2 patients with specific ABCB11 variants resulting in non-functional or complete absence of bile salt export pump (BSEP) protein.
  - The recommended dosage is 570 mcg/kg twice daily 30 minutes before a meal. The starting dose is 285 mcg/kg orally 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 38 mg (4 mL) per day. Refer to the product labeling Table 2: Volume per Dose (mL) by Patient Weight.

Dose Adjustments

- **Hepatic Impairment:** Interrupt treatment if new onset hepatic function abnormalities occur. Once hepatic function returns to baseline or stabilizes at a new baseline, consider restarting maralixibat at 190 mcg/kg/day and increase to 380 mcg/kg/day as tolerated. Consider permanent discontinuation if abnormalities in liver tests recur or symptoms consistent with clinical hepatitis are observed. Permanently discontinue treatment if a patient experiences a hepatic decompensation event (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).
- **Renal Impairment:** Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

Drug Availability

- 9.5 mg/mL oral solution in a 30 mL amber plastic bottle [285 mg per bottle]

- Store between 20°C and 25°C (68°F and 77°F), excursion permitted between 15°C and 30°C (59°F and 86°F). Discard any remaining maralixibat 45 days after first opening of bottle. Always store with cap on the bottle.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy)

Precautions/Warnings

- **Hepatotoxicity:** Obtain baseline liver tests and monitor patients frequently for the first 6 to 8 months after starting therapy, and as clinically indicated thereafter during treatment. If liver test abnormalities or signs of clinical hepatitis occur, consider dose reduction or treatment interruption. For persistent or recurrent liver test abnormalities relative to baseline, discontinuation Livmarli. Monitor patients with compensated cirrhosis frequently. Permanently discontinue Livmarli if hepatic decompensation event occurs.
- **Gastrointestinal Adverse Reactions**: Consider reducing the dosage or interrupting treatment if a patient experiences persistent diarrhea, abdominal pain, vomiting, or has diarrhea with bloody stool, vomiting, dehydration requiring treatment, or fever. If diarrhea, abdominal pain, or vomiting persists and no alternate etiology is identified, consider stopping treatment.
- **Fat-Soluble Vitamin (FSV) Deficiency**: Obtain baseline levels and monitor during treatment. Supplement if deficiency is observed. If FSV deficiency persists or worsens despite FSV supplementation, consider discontinuing treatment.
- **Bile Acid Binding Resins**: Bile acid binding resins may bind maralixibat in the gut, which may reduce efficacy. Administer bile acid binding resins (e.g., cholestyramine, colesevelam, or colestipol) at least 4 hours before or 4 hours after administration of maralixibat.
- **Hepatic Decompensation**: Maralixibat has not been studied in patients with hepatic decompensation. Discontinue permanently if a patient experiences a hepatic decompensation event (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, non chemotherapeutic, nos

ICD-10 Diagnosis Codes That Support Medical Necessity

E78.7	Disorder of bile acid and cholesterol metabolism, unspecified
K76.8	Other specified diseases of liver

Q44.71	Alagille syndrome
Q44.79	Other congenital malformations of liver

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

Odevixibat (Bylvay) Capsule, 09-J4000-09

OTHER:

None

REFERENCES:

1. Amirneni S, Haep N, Gad MA, et al. Molecular overview of progressive familial intrahepatic cholestasis. World. J Gastroenterol. 2020 Dec 21;26(47):7470-7484.
2. Ayoub MD, Kamath BM. Alagille Syndrome: Current Understanding of Pathogenesis, and Challenges in Diagnosis and Management. Clin Liver Dis. 2022;26(3):355-370.
3. Beuers U, et al. Pruritus in cholestasis: Facts and fiction. Hepatology. 2014; 60:399-407.
4. Bolia R, Goel AD, Sharma V, Srivastava A. Biliary diversion in progressive familial intrahepatic cholestasis: a systematic review and meta-analysis. Expert Rev Gastroenterol Hepatol. 2022;16(2):163-17.
5. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2024. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 03/25/24.
6. ClinicalTrials.gov. Safety and Efficacy Study of LUM001 (Maralixibat) With a Drug Withdrawal Period in Participants with Alagille Syndrome (ALGS) (ICONIC). Identifier: NCT02160782. Accessed 10/10/21 at: https://clinicaltrials.gov/ct2/show/NCT02160782.

7. Davit-Spraul, A, Gonzales, E, Baussan, C, et al. Progressive familial intrahepatic cholestasis. Orphanet J Rare Dis. 2009; 4:1.
8. Dull MM and Kremer AE. Newer approaches to the management of pruritus in cholestatic liver disease. Curr Hepatol Rep 2020; 19:86-95.
9. Ebhohon E, Chung RT. Systematic review: efficacy of therapies for cholestatic pruritus. Therap Adv Gastroenterol. 2023; 16:17562848231172829. Published 2023 May 25.
10. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. J Hepatol. 2009 Aug;51(2):237-67.
11. Gonzales E, Hardikar W, Stormon M, et al. Efficacy and safety of maralixibat treatment in patients with Alagille syndrome and cholestatic pruritus (ICONIC): a randomised phase 2 study. Lancet. 2021;398(10311):1581-1592.
12. Gunaydin M, Bozkurter Cil AT. Progressive familial intrahepatic cholestasis: diagnosis, management and treatment. Hepat Med. 2018 Sep 10; 10:95-104.
13. Hüpper MN, Pichler J, Huber WD, et al. Surgical versus Medical Management of Progressive Familial Intrahepatic Cholestasis-Case Compilation and Review of the Literature. Children (Basel). 2023;10(6):949. Published 2023 May 26.
14. Jacquemin E. Progressive familial intrahepatic cholestasis. Clin Res Hepatol Gastroenterol. 2012;36 Suppl 1: S26-S35.
15. Jacquemin E, et al. Ursodeoxycholic acid therapy in pediatric patients with progressive familial intrahepatic cholestasis. Hepatology. 1997;25(3):519-523.
16. Jones-Hughes T, Campbell J, Crathorne L. Epidemiology and burden of progressive familial intrahepatic cholestasis: a systematic review. Orphanet J Rare Dis. 2021 Jun 3;16(1):255.
17. Kamath BM, Stein P, Houwen RH, et al. Potential of ileal bile acid transporter inhibition as a therapeutic target in Alagille syndrome and progressive familial intrahepatic cholestasis. Liver Int 2020; 40:1812-1822.
18. Kohut TJ, Gilbert MA, Loomes KM. Alagille Syndrome: A Focused Review on Clinical Features, Genetics, and Treatment. Semin Liver Dis. 2021 Nov;41(4):525-537.
19. Livmarli (maralixibat chloride solution) [prescribing information]. Foster City, CA: Mirum Pharmaceuticals, Inc.; March 2024.
20. Loomes KM, Squires RH, Kelly D, et al. Maralixibat for the treatment of PFIC: Long-term, IBAT inhibition in an open-label, Phase 2 study. Hepatol Commun. 2022;6(9):2379-2390.
21. Mayo MJ, Pockros PJ, Jones D, et al. A Randomized, Controlled, Phase 2 Study of Maralixibat in the Treatment of Itching Associated with Primary Biliary Cholangitis. Hepatol Commun. 2019 Feb 1;3(3):365-381.
22. Menon J, Shanmugam N, Vij M, Rammohan A, Rela M. Multidisciplinary Management of Alagille Syndrome. J Multidiscip Healthc. 2022 Feb 23; 15:353-364. doi: 10.2147/JMDH.S295441.
23. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 03/25/24.

24. Muntaha HST, Munir M, Sajid SH, et al. Ileal Bile Acid Transporter Blockers for Cholestatic Liver Disease in Pediatric Patients with Alagille Syndrome: A Systematic Review and Meta-Analysis. J Clin Med. 2022;11(24):7526. Published 2022 Dec 19.
25. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 2024 Mar 25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
26. Vander Does A, Levy C, Yosipovitch G. Cholestatic Itch: Our Current Understanding of Pathophysiology and Treatments. Am J Clin Dermatol. 2022;23(5):647-659.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 09/13/23.

GUIDELINE UPDATE INFORMATION:

01/01/22	New Medical Coverage Guideline.
10/15/22	Review and revision to guidelines consisting of updates to the Position Statement.
05/15/23	Revision to guidelines consisting of updates to the description, position statement, dosage/administration, and referenced based on the expanded approval to include patients aged 3 months to 12 months.
10/01/23	Revision: Added ICD-10 code Q44.71 and deleted code Q44.7.
10/15/23	Review and revision to guidelines consisting of updates to the description and references.
06/15/234	Revision to guidelines consisting of updates to the description, position statement, dosage/administration, precautions, billing/coding, and references based on the new FDA-approved indication for PFIC.