Drug Coverage Policy

Effective Date.....9/15/2026
Coverage Policy Number.....IP0341
Policy Title.....Livmarli

Hepatology – Livmarli

- Livmarli™ (maralixibat oral solution and tablets – Mirum)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Livmarli, an ileal bile acid transporter (IBAT) inhibitor, is indicated for the treatment of:[1]

- Cholestatic pruritus in patients ≥ 3 months of age with **Alagille syndrome** (ALGS).
- Cholestatic pruritus in patients ≥ 12 months of age with **progressive familial intrahepatic cholestasis** (PFIC).

Disease Overview

ALGS is a rare liver disease defined by genetic deletion or genetic pathogenic variants affecting bile acid transporters (e.g., deletion or variant of the JAG1 gene or NOTCH2 gene).[2-4] **PFIC** is a group of rare, autosomal recessive liver diseases defined by genetic pathogenic variants affecting bile acid transporters (e.g., variants of the ATP8B1 gene, ABCB11 gene, ABCB4 gene, TJP2 gene, NR1H4 gene, or MYO5B gene).[5-7] Progression of both diseases can cause liver fibrosis, cirrhosis, or end-stage liver disease and leads to death at an early age in life (infancy to adolescence). Cholestasis, jaundice, and pruritus are common symptoms in patients with PFIC and ALGS.[2,5] Although the complete mechanism by which Livmarli improves pruritus in these patients is unknown, it may involve inhibition of the IBAT, which results in decreased reuptake of bile salts, as observed by a decrease in serum bile acids.[1]

Cholestyramine, rifampicin, and ursodeoxycholic acid (ursodiol) have been used off-label for decades to alleviate symptoms related to PFIC and ALGS.[7-9] Additionally, cholestyramine, fenofibrate, ursodeoxycholic acid, rifampicin, naltrexone, and sertraline are recommended in clinical practice guidelines from the European Association for the Study of the Liver (2024).[10]

Clinical Efficacy

The efficacy of Livmarli for ALGS was evaluated in one study that included an 18-week open-label treatment period, followed by a 4-week randomized, double-blind, placebo-controlled drug withdrawal period.[1] The study was conducted in 31 pediatric patients with ALGS (1 year to 15 years of age) with cholestasis and pruritus. All enrolled patients had a JAG1 genetic variant, elevated serum bile acid concentration, and presence of at least moderate pruritus at baseline. Approximately 90.3% of patients were receiving at least one medication to treat pruritus at study entry. Patients treated with Livmarli demonstrated greater improvement in pruritus compared to placebo. Safety and tolerability in infants less than 1 year of age was assessed in a 13-week, open label, phase II study of 12 patients. Livmarli was well-tolerated with treatment emergent adverse events, which were mostly Grade 1 and unrelated to therapy.

The efficacy of Livmarli for PFIC was evaluated in one 26-week, randomized, placebo-controlled pivotal trial.[1] Efficacy was evaluated in 64 patients (12 months to 17 years of age) 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. Most patients were on stable ursodeoxycholic acid (89.1%) or rifampicin (51.6%) therapy at baseline. Patients treated with Livmarli demonstrated greater improvement in pruritus compared with placebo.

Safety

Livmarli was not evaluated in patients with decompensated cirrhosis.[1] Monitor for liver test abnormalities; permanently discontinue Livmarli if a patient progresses to clinically significant portal hypertension or experiences a hepatic decompensation event (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Livmarli. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Livmarli as well as the monitoring required for adverse events and long-term efficacy, approval requires Livmarli to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, prescription receipts and/or other information. All documentation must include patient-specific identifying information.

Livmarli is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Alagille Syndrome**. Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi and vii):
     - **i.** Patient is ≥ 3 months of age; AND
     - **ii.** Patient has moderate-to-severe pruritus, according to the prescriber; AND
     - **iii.** Diagnosis of Alagille syndrome was confirmed by genetic testing demonstrating a *JAG1* or *NOTCH2* deletion or pathogenic variant**[documentation required]**; AND
     - **iv.** Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory; AND
     - **v.** Patient has tried at least two systemic medications for Alagille syndrome, unless contraindicated; AND
       Note: Systemic medications for Alagille syndrome include cholestyramine, fenofibrate, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol).
     - **vi.** Patient does not currently have, or have a history of a hepatic decompensation event; AND
       Note: Examples of a hepatic decompensation event include gastroesophageal varices, variceal hemorrhage, ascites, and hepatic encephalopathy.
     - **vii.** The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in Alagille syndrome.
   - **B)** Patient is Currently Receiving Livmarli. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient does not currently have, or have a history of a hepatic decompensation event; AND
       Note: Examples of a hepatic decompensation event include gastroesophageal varices, variceal hemorrhage, ascites, and hepatic encephalopathy.
     - **ii.** Patient had response to therapy, as determined by the prescriber; AND
       Note: Examples of response to therapy include decrease in serum bile acids and decrease in pruritus.
     - **iii.** The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in Alagille syndrome.

2. **Progressive Familial Intrahepatic Cholestasis**. Approve for the duration noted if the patient meets ONE of the following(A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi and vii):
     - **i.** Patient is ≥ 12 months of age; AND
     - **ii.** Patient has moderate-to-severe pruritus, according to the prescriber; AND
     - **iii.** Diagnosis of progressive familial intrahepatic cholestasis was confirmed by genetic testing demonstrating a pathogenic gene variant affiliated with progressive familial intrahepatic cholestasis **[documentation required]**; AND
       Note: Gene variants affiliated with progressive familial intrahepatic cholestasis include the *ATP8B1* gene*, ABCB11* gene*, ABCB4* gene*, TJP2* gene*, NR1H4* gene*,* and *MYO5B* gene.

iv. Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory; AND

v. Patient has tried at least two systemic medications for progressive familial intrahepatic cholestasis, unless contraindicated; AND
Note: Systemic medications for progressive familial intrahepatic cholestasis include cholestyramine, fenofibrate, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol).

vi. Patient does not currently have, or have a history of a hepatic decompensation event; AND
Note: Examples of a hepatic decompensation event include gastroesophageal varices, variceal hemorrhage, ascites, and hepatic encephalopathy.

vii. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in progressive familial intrahepatic cholestasis.

B) Patient is Currently Receiving Livmarli. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient does not currently have, or have a history of a hepatic decompensation event; AND
Note: Examples of a hepatic decompensation event include gastroesophageal varices, variceal hemorrhage, ascites, and hepatic encephalopathy.

ii. Patient had response to therapy, as determined by the prescriber; AND
Note: Examples of response to therapy include decrease in serum bile acids and decrease in pruritus.

iii. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in progressive familial intrahepatic cholestasis.

Conditions Not Covered

Livmarli for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Livmarli™ oral solution and tablets [prescribing information]. Foster City, CA: Mirum; April 2025.
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3. Alagille syndrome. US National Library of Medicine. Available at: https://medlineplus.gov/genetics/condition/alagille-syndrome. Accessed on June 16, 2026.
4. Treatment for Alagille syndrome. National Institute of Diabetes and Digestive and Kidney Diseases. US Department of Health and Human Services. Updated January 2019. Available at: https://www.niddk.nih.gov/health-information/liver-disease/alagille-syndrome/treatment. Accessed on June 16, 2026.
5. Davit-Spraul, A, Gonzales, E, Baussan, C, et al. Progressive familial intrahepatic cholestasis. *Orphanet J Rare Dis*. 2009;4:1.
6. 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.
7. Gunaydin M, Bozkurter Cil AT. Progressive familial intrahepatic cholestasis: diagnosis, management, and treatment. *Hepat Med*. 2018 Sep 10;10:95-104.
8. van der Woerd WL, Houwen RH, van de Graaf SF. Current and future therapies for inherited cholestatic liver diseases. *World J Gastroenterol*. 2017 Feb 7;23(5):763-775.

9. Diaz-Frias J, Kondamudi NP. Alagille Syndrome. [Updated 2026 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507827/. Accessed on June 16, 2026.
10. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on genetic cholestatic liver diseases. *J Hepatol*. 2024 Aug;81(2):303-325.

Revision Details

Summary of Changes	Review Date	Effective Date
No criteria changes	10/31/2024	1/1/2025
Added oral tablets to coverage policy. **Progressive Familial Intrahepatic Cholestasis:** The criterion for age was changed from ≥ 12 years to ≥ 12 months of age to align with FDA indication expansion for age. Added oral tablets to coverage policy. Added "documentation required" as noted in criteria.	6/18/2025	7/15/2025
Policy Title. **Updated** from "Maralixibat" **to** "Hepatology – Livmarli" **Alagille Syndrome** **Added** "according to the prescriber" to moderate-to-severe pruritus criteria **Updated** "Documented failure, contraindication, or intolerance to TWO systemic medications for Alagille syndrome (for example, cholestyramine, rifampicin, ursodeoxycholic acid [ursodiol])" **to** "Patient has tried at least two systemic medications for Alagille syndrome, unless contraindicated; AND Note: Systemic medications for Alagille syndrome include cholestyramine, fenofibrate, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol)" **Added** criteria for patients currently receiving Livmarli **Progressive Familial Intrahepatic Cholestasis** **Added** documentation requirements to Diagnosis of progressive familial intrahepatic cholestasis criteria. **Added** fenofibrate to note of systemic medications **Added** criteria for patients currently receiving Livmarli	9/11/2025	11/1/2025

Alagille Syndrome: For initial therapy and in a patient currently receiving treatment, the requirement that the patient does not have cirrhosis or portal hypertension was removed. In the note listing examples of a hepatic decompensation event, gastroesophageal varices was added. **Progressive Familial Intrahepatic Cholestasis:** For initial therapy and in a patient currently receiving treatment, the requirement that the patient does not have cirrhosis or portal hypertension was removed. In the note listing examples of a hepatic decompensation event, gastroesophageal varices was added.	8/6/2026	9/15/2026

The policy effective date is in force until updated or retired.

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