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5.50.032

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Gastrointestinal Agents	**Original Policy Date:**	October 22, 2021
Subject:	Livmarli	**Page:**	1 of 5

Last Review Date: December 13, 2024

Livmarli

Description

Livmarli (maralixibat)

Background
Livmarli (maralixibat) is an inhibitor of the ileal bile acid transporter (IBAT). IBAT is almost completely responsible for the reabsorption of bile acid from the ileum, returning biliary products to systemic circulation. Inhibition of this process promotes elimination of bile acid and reduces pruritus associated with cholestatic disease (1).

Regulatory Status
FDA-approved indications: Livmarli is an ileal bile acid transporter (IBAT) inhibitor indicated for: (1)

- the treatment of cholestatic pruritus in patients 3 months of age and older with Alagille syndrome (ALGS).
- the treatment of cholestatic pruritus in patients 12 months 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.

Livmarli treatment is associated with a potential for drug-induced liver injury. Liver tests should be obtained at baseline and monitored during treatment. Livmarli is contraindicated in patients with prior or active hepatic decompensation events (1).

Livmarli also has warnings regarding gastrointestinal adverse reactions and fat-soluble vitamin (FSV) deficiency. Patients should obtain baseline levels of fat-soluble vitamins and be monitored for FSV deficiency throughout treatment (1).

Livmarli may increase the risk of propylene glycol toxicity in pediatric patients less than 5 years of age. The total daily intake of propylene glycol should be considered for managing the risk of propylene glycol toxicity. Patients should be monitored for signs of potential propylene glycol toxicity, including hemolysis, hyperosmolarity with anion gap metabolic acidosis, acute kidney injury, and CNS toxicity. Discontinue Livmarli if toxicity is suspected (1).

The Rare Disease Database includes diagnostic criteria for Alagille syndrome, including characteristic symptoms, bile duct paucity, and genetic testing (2).

The safety and effectiveness of Livmarli in patients less than 3 months of age with ALGS have not been established. The safety and effectiveness of Livmarli in pediatric patients less than 12 months of age with PFIC have not been established (1).

Related policies
Bylvay

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Livmarli may be considered **medically necessary** if the conditions indicated below are met.

Livmarli may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Cholestatic pruritus associated with Alagille syndrome (ALGS)
    a. 3 months of age or older

b. Diagnosis has been confirmed by **ONE** of the following:
    i. Genetic testing (e.g., JAGGED1 mutation)
    ii. Patient has bile duct paucity **AND** at least 3 major clinical features of ALGS (e.g., cholestasis, cardiac defect, skeletal abnormality, ophthalmic abnormality, or characteristic facial features)
2. Cholestatic pruritus associated with progressive familial intrahepatic cholestasis (PFIC)
    a. 12 months of age or older
    b. **NO** PFIC type 2 with ABCB11 variants causing non-functional or complete absence of bile salt export pump protein

AND ALL of the following:
1. **NO** clinically significant portal hypertension or decompensated cirrhosis
2. Inadequate treatment response, intolerance, or contraindication to **ONE** of the following:
    a. Cholestyramine
    b. Rifampin
    c. Ursodeoxycholic acid (UDCA)
3. Patient has had baseline liver function tests (LFTs) and serum fat-soluble vitamin (FSV) levels performed
4. Prescriber agrees to monitor liver function tests (LFTs) and serum fat-soluble vitamin (FSV) levels during treatment

Prior–Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Cholestatic pruritus associated with Alagille syndrome (ALGS)
    a. 3 months of age or older
2. Cholestatic pruritus associated with progressive familial intrahepatic cholestasis (PFIC)
    a. 12 months of age or older

AND ALL of the following:
1. Improvement in pruritus symptoms, or observed improvement in scratching

2. **NO** clinically significant portal hypertension or decompensated cirrhosis
3. Prescriber agrees to monitor LFTs and serum FSV levels during treatment

Policy Guidelines

Pre–PA Allowance

None

Prior - Approval Limits

Quantity

Diagnosis	Strength	Quantity
Alagille Syndrome (ALGS)	9.5 mg/mL	28.5 mg (3 mL) per day **OR**
Progressive Familial Intrahepatic Cholestasis (PFIC)	19 mg/mL	38 mg (2 mL) per day

Duration 12 months

Prior–Approval *Renewal* Limits

Same as above

Rationale

Summary

Livmarli is an ileal bile acid transport (IBAT) inhibitor indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) or progressive familial intrahepatic cholestasis (PFIC). Current warnings include gastrointestinal adverse reactions, hepatotoxicity, and fat-soluble vitamin deficiency. Livmarli is contraindicated in patients with prior or active hepatic decompensation events. The safety and effectiveness of Livmarli in patients less than 3 months of age with ALGS have not been established. The safety and effectiveness of Livmarli in pediatric patients less than 12 months of age with PFIC have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Livmarli while maintaining optimal therapeutic outcomes.

References

1. Livmarli [package insert]. Foster City, CA: Mirum Pharmaceuticals, Inc.; July 2024.
2. National Organization for Rare Disorders (NORD). Alagille syndrome. Rare Disease Database. https://rarediseases.org. Published 2020.

Policy History

Date	Action
October 2021	Addition to PA
December 2021	Annual review
March 2022	Annual editorial review and reference update. To match Bylvay: Added rifampicin to list of medication options, and added requirement that patient must not have cirrhosis, clinically significant portal hypertension, or hepatic decompensation for approval and renewal requirements. Per SME, added initiation requirement for the diagnosis to be confirmed by genetic testing or by bile duct paucity and at least 3 major clinical features
April 2023	Per PI update, reduced age requirement from 1 year and older to 3 months and older. Changed policy number to 5.50.032
June 2023	Annual review and reference update
March 2024	Per PI update, added indication of cholestatic pruritus associated with PFIC and increased quantity limit to 4 mL per day. Also revised requirement to “no clinically significant portal hypertension or decompensated cirrhosis”
June 2024	Annual review
August 2024	Per PI update, lowered age for PFIC to 12 months and older. Added warning regarding propylene glycol toxicity. Revised quantity limits. Revised rifampicin to rifampin
December 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.