Pharmacy Policy Bulletin: J-1151 Livmarli (maralixibat) – Commercial and Healthcare Reform	
Number: J-1151	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Quantity Limits (1., 2., 3., or 4.):** **1.** Rx Mgmt Quantity Limits = Safety/Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Quantity Limits = MRXC = Yes **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1151-007	**Original Date:** 12/01/2021
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Livmarli (maralixibat)
FDA-Approved Indication(s):	• Treatment of cholestatic pruritus in patients 3 months of age or older with Alagille syndrome (ALGS). • 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 nonfunctional or complete absence of bile salt export pump (BSEP) protein.

Background:	• Livmarli (maralixibat) is a self-administered, oral ileal bile acid transporter (IBAT). • Alagille syndrome (ALGS) is a rare, autosomal dominant multisystem disorder associated with disrupted Notch signaling, which leads to the abnormal development of the intrahepatic bile ducts. The predominating liver-related clinical features of ALGS are chronic cholestasis, jaundice, and cirrhosis with symptoms typically developing around 3 months of life. • Progressive familial intrahepatic cholestasis (PFIC) is a disorder that causes progressive liver disease and liver failure. In PFIC, the ability of liver cells to secrete bile is impaired, causing an excess of bile in liver cells and subsequently

liver disease. There are three types of PFIC: PFIC1, PFIC2, and PFIC3. Each type has a different genetic cause, and they also cause shortages of different proteins needed for normal liver function. PFIC causes symptoms of liver disease, including pruritis.

- Pruritus has been shown to affect 59%–88% of ALGS patients, with up to 45% reporting severe pruritus. This unrelenting itching is associated with additional symptoms, such as skin damage, sleep problems, mood disturbances, and reduced health-related quality of life. One-third of parents recognized itching as the characteristic of ALGS that affected their children most.
- The pathophysiology of pruritus in patients with ALGS is not completely known, but it has been hypothesized to be caused by the accumulation of toxic bile acids. The benefit observed with Livmarli may be due to the reversible inhibition of the IBAT, which decreases the reabsorption of bile acids from the terminal ileum. All patients in the clinical trial for Livmarli had elevated levels of serum bile acids.
- All patients in the clinical trial for Livmarli had *JAGGED1* mutation. A small percentage (approximately 2%) of patients with ALGS have a mutation of the *NOTCH2* gene.
- ICD-10 Code Information:
    - ICD-10: K76.8 “Other specified diseases of the liver” may apply to primary familial intrahepatic cholestasis (PFIC); however, the prescriber must specify the diagnosis.
- Initial authorization duration is to assess efficacy and safety. Liver tests including alanine transaminase (ALT), aspartate transaminase (AST), total and direct bilirubin should be monitored at baseline and during treatment for the development of liver-related adverse events.
- Prescribing Considerations:
    - Livmarli is available as an oral solution in 2 strengths: 9.5 mg/mL and 19 mg/mL, as well as oral tablets in 10 mg, 15 mg, 20 mg, and 30 mg strengths. Livmarli 9.5 mg/mL is for the treatment of ALGS. Livmarli 19 mg/mL is for the treatment of PFIC. The 2 strengths should not be substituted one for another when treating PFIC patients. Livmarli tablets can be used for treatment of both ALGS and PFIC in patients weighing 25 kg and above who can swallow tablets.
    - Livmarli for ALGS should be dosed starting at 190 mcg/kg orally once daily for one week and increased to 380 mcg/kg once daily as tolerated. The maximum recommended dose is 3 mL (28.5 mg) per day for the oral solution and 30 mg per day for the tablets.
    - Livmarli for PFIC should be dosed starting at 285 mcg/kg orally once and should be increased to 570 mcg/kg twice daily as tolerated. The maximum recommended daily dose is 38 mg (2 mL) for the oral solution and 40 mg per day for the tablets.
    - Livmarli oral solution contains propylene glycol. Patients less than 5 years of age are at highest risk for propylene glycol toxicity, and a safe level for propylene glycol exposure with repeated administration has not been established for pediatric patients less than 5 years of age. Monitor patients for signs of propylene glycol toxicity. Discontinue if toxicity is suspected.
    - Do not use Livmarli oral solution 100 days after first opening the bottle.
    - Livmarli has warnings and/or precautions for liver test abnormalities, gastrointestinal adverse reactions, and fat-soluble deficiency.
    - Livmarli should be prescribed by a hepatologist or prescriber specialized in treating ALGS.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Livmarli may be approved when all of the following criteria are met **(A. through D.):**

A. The member meets one (1) of the following criteria **(1. or 2.)**:
- **1.** The member has a diagnosis of Alagille syndrome (ICD-10: Q44.71) confirmed by genetic testing demonstrating a *JAGGED1* or *NOTCH2* deletion or mutation and meets the following criterion **(a. and b.)**:
  - **a.** The member is 3 months of age or older.
  - **b.** The member meets one (1) of the following criteria **(i. or ii.)**:
    - **i.** The member is using Livmarli oral solution 9.5 mg/mL
    - **ii.** If the request is for Livmarli oral tablets, the member weighs ≥ 25 kg.
- **2. B)** The member has a diagnosis of progressive familial intrahepatic cholestasis (PFIC) (no ICD-10 code) confirmed by genetic testing and meets all of the following criteria **(a., b., and c.)**:
  - **a.** The member is 12 months of age or older.
  - **b.** The member does not have PFIC type 2 with an ABCB11 variant resulting in nonfunctional or absent bile salt export pump (BSEP) protein.
  - **c.** The member meets one (1) of the following criteria **(i. or ii.):**
    - **i.** The member is using Livmarli oral solution 19 mg/mL
    - **ii.** If the request is for Livmarli oral tablets, the member weighs ≥ 25 kg

B. The member has elevated serum bile acid levels above the laboratory reference range.

C. The provider attests that the member experiences cholestatic pruritus explained only by liver disease.

D. The member does not have any of the following diagnoses **(1., 2., and 3.):**
- **1.** Decompensated cirrhosis
- **2.** History of hepatic decompensation event
- **3.** Portal hypertension

II. Reauthorization

When a benefit, reauthorization of Livmarli may be approved when all of the following criteria are met **(A., B., and C)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy as evidenced by both of the following **(1. and 2.):**
- **1.** Decrease in total serum bile acid levels from baseline
- **2.** Improvement in pruritus

B. The prescriber attests that the member has not progressed to any of the following **(1., 2., or 3.):**
- **1.** Cirrhosis
- **2.** Experienced a hepatic decompensation event
- **3.** Portal hypertension

C. The member meets one (1) of the following criteria (**1. or 2.)**:
- **1.** The member is using Livmarli 9.5 mg/mL or oral tablets for the diagnosis of Alagille Syndrome.
- **2.** The member is using Livmarli 19 mg/mL or oral tablets for the diagnosis of PFIC.

III. Quantity Limits

When a benefit, additional quantities of Livmarli oral solution may be approved if the member meets all of the following criteria **(A. and B.):**

A. The member's weight is documented.

B. For quantities more than 1 bottle per month, Livmarli may be authorized in quantities as follows:

Alagille Syndrome 9.5 mg/mL Solution (for ALGS)		**Progressive Familial Intrahepatic Cholestasis 19 mg/mL Solution (for PFIC)**	
Patient Weight	**Maintenance Dosing (380 mcg/kg daily)**	**Patient Weight**	**Maintenance Dosing (570 mcg/kg twice daily)**

5 kg – 29 kg	1 bottle (30 mL) per month*	5 kg – 19 kg	1 bottle (30 mL) per month*
30 kg – 49 kg	2 bottles (60 mL) per month	20 kg – ≥ 60 kg	2 bottles (60 mL) per month
≥ 50 kg	3 bottles (90 mL) per month		

*The quantity limit of Livmarli is coded at 1 bottle (30 mL) per 25 days.

When a benefit, additional quantities of Livmarli oral tablets may be approved if the member meets all of the following criteria **(A. and B.)**:

A. The member's weight is documented.
B. The member has a diagnosis of PFIC which requires twice daily dosing.

Alagille Syndrome (ALGS) 10 mg, 15 mg, 20 mg, and 30 mg tablets		**Progressive Familial Intrahepatic Cholestasis (PFIC) 10 mg, 15 mg, 20 mg, and 30 mg tablets**	
Patient Weight	**Maintenance Dosing (380 mcg/kg daily)**	**Patient Weight**	**Maintenance Dosing (570 mcg/kg twice daily)**
25 kg – 32 kg	10 mg*once daily	25 kg – 32 kg	15 mg twice daily – (2 of the 15 mg tablets)
33 kg – 43 kg	15 mg*once daily	33 kg – 43 kg	20 mg twice daily – (2 of the 20 mg tablets)
44 kg – 65 kg	20 mg*once daily	44 kg or higher	20 mg twice daily – (2 of the 20 mg tablets)
66 kg or higher	30 mg*once daily		

*The quantity limit of Livmarli tablets is coded at 1 tablet per day.

IV. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization

- Commercial and HCR Plans: If approved, up to a 6 month authorization may be granted.

Reauthorization

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Livmarli [maralixibat]. Foster City, CA: Mirum Pharmaceuticals, Inc.; April 2025.

2. Kamath BM, Baker A, Houwen R, et al. Systematic review: the epidemiology, natural history, and burden of Alagille syndrome. *J Pediatr Gastroenterol Nutr.* 2018;67(2):148-156.
3. Ameur SB, Chabchoub I, Telmoudi J, et al. Management of cholestatic pruritus in children with Alagille syndrome: case report and literature review. *Arch Pediatr*. 2016;23(12):1247-1250.
4. Pollock G, Minuk GY. Diagnostic considerations for cholestatic liver disease. *J Gastroenterol Hepatol*. 2017;32(7):1303-1309.
5. MedlinePlus. Progressive familial intrahepatic cholestasis. Available at: https://medlineplus.gov/genetics/condition/progressive-familial-intrahepatic-cholestasis/. Accessed February 11, 2025
6. Verkade HJ, Felzen A, Keitel V, et al. EASL Clinical Practice Guidelines on genetic cholestatic liver diseases. *J Hepatol*. 2024;81(2):303-325.