UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 2262-6
Program	Prior Authorization/Medical Necessity
Medication	Livmarli™ (maralixibat)
P&T Approval Date	11/2021, 1/2022, 1/2023, 5/2023, 5/2024, 9/2024
Effective Date	12/1/2024

1. Background:

Livmarli (maralixibat) is an ileal bile acid transporter inhibitor indicated for the treatment of cholestatic pruritis in patients 12 months of age and older with progressive familial intrahepatic cholestasis (PFIC). Livmarli is also indicated for the treatment of cholestatic pruritis in patients 3 months of age and older with Alagille syndrome (ALGS).

PFIC is a heterogeneous group of liver disorders of autosomal recessive inheritance, characterized by an early onset of cholestasis (usually during infancy) with pruritus and malabsorption, which rapidly progresses and ends up as liver failure. Pruritus is the most obvious and the most unbearable symptom in cholestasis. It has been proposed that it is induced by the stimulation of nonmyelinated subepidermal free nerve ends because of increased serum bile acids.

ALGS is a rare genetic disorder caused by a mutation in the JAG1 or Notch2 genes which are involved in embryonic development in utero. In ALGS patients, multiple organ systems may be affected by the mutation. In the liver, the mutation causes the bile ducts to abnormally narrow, malform and reduce in number, leading to bile acid accumulation, cholestasis, and ultimately progressive liver disease. The cholestatic pruritus experienced by patients with ALGS is among the most severe in any chronic liver disease and is present in most affected children by the third year of life.

Conventional treatments for pruritis associated with PFIC or Alagille syndrome include uroseoxycholic acid (UCDA), antihistamines (e,g., diphenhydramine), bile acid sequestrants (e.g., cholestyramine), rifampin, naltrexone and sertraline.

Limitation 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.

2. Coverage Criteria[a]:

A. Progressive Familial Intrahepatic Cholestasis

1. **Initial Authorization**

a. **Livmarli** will be approved based upon **all** of the following criteria:

(1) Diagnosis of progressive familial intrahepatic cholestasis (PFIC)

-AND-

(2) Patient does not have a ABCB11 variant resulting in non-functional or complete absence of bile salt export pump (BSEP) protein

-AND-

(3) Patient is experiencing moderate to severe pruritus associated with PFIC.

-AND-

(4) Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory.

-AND-

(5) Patient has had an inadequate response to at least **two** conventional treatments for the symptomatic relief of pruritus (e.g., uroseoxycholic acid, diphenhydramine, cholestyramine, rifampin, naltrexone, and sertraline).

-AND-

(6) Prescribed by a gastroenterologist or hepatologist.

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Livmarli** will be approved based on **both** of the following criteria:

(1) Documentation of positive clinical response to Livmarli therapy (e.g., reduced serum bile acids, improved pruritis and less sleep disturbance)

-AND-

(2) Prescribed by a gastroenterologist or hepatologist.

Authorization will be issued for 12 months.

B. Alagille Syndrome

1. **Initial Authorization**

a. **Livmarli** will be approved based upon **all** of the following criteria:

(1) Diagnosis of Alagille syndrome (ALGS)

-AND-

(2) Confirmation of diagnosis by presence of the JAG1 or Notch2 gene mutation

-AND-

(3) Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory.

-AND-

(4) Patient is experiencing moderate to severe pruritis associated with ALGS

-AND-

(5) Patient has had an inadequate response to at least **two** conventional treatments for the symptomatic relief of pruritus (e.g., uroseoxycholic acid, diphenhydramine, cholestyramine, rifampin, naltrexone, and sertraline).

-AND-

(6) Prescribed by a gastroenterologist or hepatologist.

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Livmarli** will be approved based on **both** of the following criteria:

(1) Documentation of positive clinical response to Livmarli therapy (e.g., reduced serum bile acids, improved pruritis)

-AND-

(2) Prescribed by a gastroenterologist or hepatologist.

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. Reference:

1. Livmarli [package insert]. Foster City, CA: Mirum Pharmaceuticals, Inc.; July 2024.

2. 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.
3. Miethke AG, Moukarzel A, Porta G, et al. Maralixibat in progressive familial intrahepatic cholestasis (MARCH-PFIC): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial [published correction appears in Lancet Gastroenterol Hepatol. 2024 Jul;9(7):e10.
4. Chowdhury JR, Chowdhury NR. Inherited disorders associated with conjugated hyperbilirubinemia in adults. In: Post TW, ed. *UpToDate*. UpToDate, 2024. Accessed July 9, 2024. Inherited disorders associated with conjugated hyperbilirubinemia in adults - UpToDate
5. Kohut TJ, Loomes KM. Alagille syndrome. In: Post TW, ed. *UpToDate.* UpToDate, 2024. Accessed July 9, 2024. Alagille syndrome - UpToDate

Program	Prior Authorization/Medical Necessity - Livmarli (maralixibat)
Change Control	
11/2021	New program.
1/2022	Updated coverage criteria to require trial of at least two medications for pruritis.
1/2023	Annual review with no changes to coverage criteria.
5/2023	Updated background with expanded indication in ALGS patients 3 months of age and older. No change to coverage criteria. Updated reference.
5/2024	Annual review. Added coverage criteria for new PFIC indication. Updated authorization durations to 12 months for ALGS indication. Updated background and references.
9/2024	Updated background with expanded PFIC indication in patients 12 months to 4 years of age. Updated examples of conventional treatment within initial authorization criteria for both PFIC and ALGS. Updated references.