UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 2262-4
Program	Prior Authorization/Medical Necessity
Medication	Livmarli™ (maralixibat)
P&T Approval Date	11/2021, 1/2022, 1/2023, 5/2023
Effective Date	8/1/2023; Oxford only: 8/1/2023

1. Background:

Livmarli (maralixibat) is an ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of cholestatic pruritis in patients with Alagille syndrome (ALGS) 3 months of age and older.

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 ALGS include: ursodeoxycholic acid (ursodiol), rifampin, and bile acid sequestrants (e.g., cholestyramine, colesevelam).

2. Coverage Criteria[a]:

A. Initial Authorization

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

   a. Diagnosis of Alagille syndrome (ALGS) confirmed by presence of the JAG1 or Notch2 gene mutation

   -AND-

   b. **One** of the following:

      1) Total serum bile acid > 3x the upper limit of normal
      2) Conjugated bilirubin > 1 mg/dL.
      3) Fat soluble vitamin deficiency otherwise unexplainable.
      4) GGT > 3x the upper limit of normal
      5) Intractable pruritus explainable only by liver disease.

   -AND-

   c. Patient is experiencing moderate to severe pruritis

   -AND-

   d. Patient has had an inadequate response to at least **two** medications to treat pruritus (e.g., ursodeoxycholic acid, rifampin, cholestyramine, colesevelam).

-AND-

e. Prescribed by a hepatologist.

Authorization will be issued for 6 months.

B. Reauthorization

1. **Livmarli** will be approved based on **all** the following criterion:

   a. Documentation of positive clinical response to Livmarli therapy (e.g., reduced serum bile acids, reduced pruritis severity score)

-AND-

   b. Prescribed by a 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.; March 2023.
2. Erlichman J, Loomes KM. Cause of cholestasis in neonates and young infants. In: Post TW, ed. *UpToDate*. UpToDate, 2021. Accessed October 4, 2021. https://www.uptodate.com/contents/causes-of-cholestasis-in-neonates-and-young-infants
3. Clinicaltrials.gov. A Multicenter Extension Study to Evaluate the Long-Term Safety and Durability of the Therapeutic Effect of LUM001, an Apical Sodium-Dependent Bile Acid Transporter Inhibitor (ASBTi), in the Treatment of Cholestatic Liver Disease in Pediatric Subjects With Alagille Syndrome. Trial: NCT02057692. 2019;Status: Completed. Available from: https://clinicaltrials.gov/ct2/show/NCT02117713
4. Clinicaltrials.gov. Safety and Efficacy Study of LUM001 With a Drug Withdrawal Period in Participants With Alagille Syndrome (ALGS) (ICONIC). NCT02160782,. 2019;Status: Completed. Available from: https://clinicaltrials.gov/ct2/show/NCT02160782.

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.