MEDICAL MUTUAL®

Drug Policy

Policy: SD	Livmarli (maralixibat)	Annual Review Date: 05/16/2024 Last Revised Date: 05/16/2024

OVERVIEW

Livmarli is an ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of cholestatic pruritis in patients 1 year of age and older with Alagille syndrome (ALGS). Livmarli is also indicated for progressive familial intrahepatic cholestasis. Livmarli was not evaluated in patients with cirrhosis. Alagille syndrome is a rare liver disease defined by genetic deletion or mutation affecting bile acid transporters (e.g. deletion or mutation of the JAG1 gene or NOTCH2 gene).

POLICY STATEMENT

This policy involves the use of Livmarli. Prior authorization is recommended for pharmacy benefit coverage of Livmarli. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

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, initial approval requires Livmarli be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Livmarli is recommended in those who meet the following criteria:

1. <u>Alagille Syndrome, initial therapy</u>

Criteria. *Patient must meet the following criteria*

- **A.** The patient is ≥ 3 months of age; AND
- **B.** The patient has moderate-to-severe pruritis, according to the prescriber; AND
- **C.** Diagnosis of Alagille syndrome was confirmed by genetic testing demonstrating a JAG1 or NOTCH2 deletion or mutation; AND
- **D.** Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory; AND

E. The patient has tried at least two systemic medication for Alagille syndrome, unless contraindicated [NOTE: systemic medications for Alagille syndrome include cholestyramine, rifampicin, and ursodiol (ursodeoxycholic acid)]; AND

F. The patient does NOT have any of the following (a, b, or c):
- **a.** Cirrhosis; OR
- **b.** Portal hypertension; OR
- **c.** History of a hepatic decompensation event; AND [NOTE: examples of a hepatic decompensation event include variceal hemorrhage, ascites, and hepatic encephalopathy]; AND

G. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in Alagille syndrome.

2. Alagille Syndrome, continuation of therapy
Criteria. *Patient must meet the following criteria*

A. The patient does not have any of the following (a, b, or c):
- **a.** Cirrhosis; OR
- **b.** Portal hypertension; OR
- **c.** History of a hepatic decompensation event [NOTE: examples of a hepatic decompensation event include variceal hemorrhage, ascites, and hepatic encephalopathy]; AND

B. The patient had a response to therapy, as determined by the prescriber [NOTE: examples of response to therapy include decrease in serum bile acids and decrease in pruritis]; AND

C. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in Alagille syndrome.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:* 1 year

3. 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 the following (i, ii, iii, iv, v, vi and vii):
- **i.** Patient is ≥ 5 years 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 gene mutation affiliated with progressive familial intrahepatic cholestasis; AND
  Note: Gene mutations 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, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol).

vi. Patient does not have any of the following (a, b, or c):
- **a)** Cirrhosis; OR
- **b)** Portal hypertension; OR
- **c)** History of a hepatic decompensation event; AND
  Note: Examples of a hepatic decompensation event include 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 have any of the following (a, b, or c):
- **a)** Cirrhosis; OR
- **b)** Portal hypertension; OR
- **c)** History of a hepatic decompensation event; AND
  Note: Examples of a hepatic decompensation event include 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 RECOMMENDED FOR APPROVAL

Livmarli has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Livmarli™ oral solution [prescribing information]. Foster City, CA: Mirum; September 2021.
2. Alagille syndrome. National Organization for Rare Disorders. Updated 2020. Available at: https://rarediseases.org/rare-diseases/alagille-syndrome/. Accessed on September 30, 2021.
3. Alagille syndrome. US National Library of Medicine. Updated April 7, 2021. Available at: https://medlineplus.gov/genetics/condition/alagille-syndrome. Accessed on September 30, 2021.
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 September 30, 2021.
5. 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.