Effective Date: 04/01/2022
Reviewed: 01/2022, 1/2023, 8/2023, 01/2024, 04/2024, 02/2025 Scope: Medicaid

SPECIALTY GUIDELINE MANAGEMENT

LIVMARLI (maralixibat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Livmarli is indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 3 months of age and older.
Livmarli is indicated for the treatment of cholestatic pruritus in patients 12 months of age and older with progressive familial intrahepatic cholestasis (PFIC).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cholestatic pruritis in Alagille syndrome (ALGS)
Authorization of 6 months may be granted for treatment of cholestatic pruritis in Alagille syndrome (ALGS) when all of the following criteria are met:
A. Member is 3 months of age or older
B. This medication must be prescribed by or in consultation with a hepatologist or gastroenterologist or a physician that specializes in Alagille Syndrome.
C. Documentation that the member has moderate to severe pruritus and drug-induced pruritus has been ruled out
D. Documentation that the member has a diagnosis of ALGS established by one of the following (see Appendix A for major clinical features of ALGS):
    1. Genetic testing (i.e., mutations in the *JAG1* or *NOTCH2* gene)
    2. Family history of a ALGS and one or more major clinical features of ALGS
    3. Bile duct paucity and three or more major Clinical features of ALGS
    4. Four or more major clinical features of a LGS
E. Documentation that the member has evidence of cholestasis defined as the presence of one or more of the following:
    I. Total serum bile acid greater than 3 times the upper limit of normal (ULN) for age
    II. Conjugated bilirubin greater than 1 mg/dL
    III. Fat soluble vitamin deficiency otherwise unexplainable
    IV. Gamma-glutamyl transferase (GGT) greater than 3 times ULN for age
    V. Intractable pruritis explainable only by liver disease
B. Documentation that the member does not have any other concomitant liver disease (e.g., cirrhosis, liver cancer) or history of a hepatic decompensation event (e.g., variceal hemorrhage, ascites, hepatic encephalopathy, portal hypertension)
C. Documentation that the member has not received a liver transplant or surgical interruption of the enterohepatic circulation (e.g., partial external biliary diversion surgery)
D. Documentation that the member experienced an inadequate treatment response or intolerance to at least two systemic medications for ALGS-related pruritus (e.g., ursodiol at a dose of 20-30 mg/kg/day, rifampin, cholestyramine, naltrexone)
E. Documentation that the member's dose will not exceed 380 mcg/kg/day or exceed a maximum daily dose of 28.5mg. Member's current weight and prescribed dose must be provided.

Pruritus in progressive familial intrahepatic cholestasis (PFIC)
Authorization of 6 months may be granted for treatment of pruritis in progressive familial intrahepatic cholestasis (PFIC) when all of the following criteria are met:
A. Member is 12 months of age or older

B. This medication must be prescribed by or in consultation with a hepatologist or gastroenterologist or a physician that specializes in progressive familial intrahepatic cholestasis
C. Documentation that the member has moderate to severe pruritus and drug-induced pruritus has been ruled out
D. Documentation that the member has a confirmed molecular diagnosis of PFIC (e.g., mutations in
E. *ATP8B1*, *ABCB11*, TJP2, MYO5B, and *ABCB4*)
Documentation that the member has serum bile acid level ≥ 100 μmol/L
F. Documentation that the member does not have any other concomitant liver disease (e.g., cirrhosis, liver cancer) or history of a hepatic decompensation event (e.g., variceal hemorrhage, ascites, hepatic encephalopathy, portal hypertension)
G. Documentation that the member has not received a liver transplant or surgical interruption of the enterohepatic circulation (e.g., partial external biliary diversion surgery)
H. Documentation that the member experienced an inadequate treatment response or intolerance to at least two systemic medications for PFIC-related pruritus (e.g., ursodiol at a dose of 20-30 mg/kg/day, rifampin, cholestyramine)
I. Documentation that the member experienced an inadequate treatment response or intolerance to Bylvay (odevixibat)
J. Documentation that the member's dose will not exceed 570 mcg/kg twice a day or exceed a maximum daily dose of 38mg/day. Member's current weight and prescribed dose must be provided.

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for all members (including new members) with documentation requesting continuation of therapy when all of the following is meet
A. Member meets all initial criteria
B. The member is experiencing benefit from therapy (e.g., improvement in pruritis and reduction in serum bile acid).
C. Member's dose will not exceed 380 mcg/kg/day or exceed a maximum daily dose of 28.5mg for ALGS or member's dose will not exceed 570 mcg/kg twice a day or exceed maximum daily dose of 38mg/day for PFIC.

IV. QUANTITY LIMIT

Livmarli oral solution 9.5mg/ml has a quantity limit of 28.5mg/3ml per day (90 ml per 30 days) for ALGS.
Livmarli oral solution 9.5mg/ml has a quantity limit of 38mg/4ml per day (120 ml per 30 days) for PFIC.

V. APPENDIX A

Major Clinical Features of ALGS

- Hepatic abnormality (e.g., cholestasis)
- Cardiac abnormality (e.g., stenosis of the peripheral pulmonary artery and its branches)
- Skeletal abnormality (e.g., butterfly vertebrae)
- Ophthalmologic abnormality (e.g., posterior embryotoxon)
- Characteristic facial features (e.g., triangular-shaped face with a broad forehead and a pointed chin, bulbous tip of the nose, deeply set eyes, and hypertelorism)
- Vascular abnormalities (e.g., intracranial bleeds, systemic vascular anomalies)
- Renal structural or functional abnormality (e.g., abnormally small size, cysts)

VI. REFERENCES

1. Livmarli [package insert]. Foster City, CA: Mirum Pharmaceuticals, Inc.; April 2024.
2. Spinner NB, Gilbert MA, Loomes KM, Krantz ID. Alagille syndrome. GeneReviews® [Internet]. December 12, 2019. Last updated December 12, 2019. Accessed October 19, 2021. https://www.ncbi.nlm.nih.gov/books/NBK1273/#__NBK1273_dtls__.
3. Genetic and Rare Diseases Information Center. Alagille syndrome. Rare Disease Database. https://rarediseases.info.nih.gov. Last updated February 2023. Accessed June 20, 2.
4. National Organization for Rare Disorders (NORD). Alagille syndrome. Rare Disease Database. https://rarediseases.org. Published 2020. Last updated January 30, 2024. . Accessed February 2025.
5. The Childhood Liver Disease Research Network. Alagille syndrome. https://childrennetwork.org/For-Physicians/Alagille-Syndrome-Information-for-Physicians. Accessed August 27, 2004.