Effective Date: 04/01/2022
Reviewed: 01/2022, 1/2023, 8/2023, 01/2024, 04/2024 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 5 years of age and older with progressive familial intrahepatic cholestasis (PFIC).

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

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: Current weight, genetic testing results confirming a diagnosis of Alagille syndrome (ALGS) (if applicable), or of progressive familial intrahepatic cholestasis (PFIC) type 1, 2, or 3 and chart notes or medical records documenting cholestasis.
B. Continuation requests: Current weight and chart notes or medical records documenting a benefit from therapy (e.g., improvement in pruritis and reduction in serum bile acid).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a hepatologist or gastroenterologist.

IV. 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. Member has moderate to severe pruritus and drug-induced pruritus has been ruled out
C. Member has a diagnosis of ALGS confirmed by either of the following:
    1. Genetic testing (i.e., presence of mutation in the *JAG1* or *NOTCH2* gene)
    2. Member has both of the following:
        i. Bile duct paucity
        ii. Three of the five major clinical features of ALGS:
            a. Cholestasis
            b. Cardiac defect (e.g., stenosis of the peripheral pulmonary artery and its branches)
            c. Skeletal abnormality (e.g., butterfly vertebrae)
            d. Ophthalmologic abnormality (e.g., posterior embryotoxon)

e. 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)

D. Member has evidence of cholestasis defined as the presence of one or more of the following:
   1. Total serum bile acid greater than 3 times the upper limit of normal (ULN) for age
   2. Conjugated bilirubin greater than 1 mg/dL
   3. Fat soluble vitamin deficiency otherwise unexplainable
   4. Gamma-glutamyl transferase (GGT) greater than 3 times ULN for age
   5. Intractable pruritis explainable only by liver disease
E. 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)
F. Member has not received a liver transplant or surgical interruption of the enterohepatic circulation (e.g., partial external biliary diversion surgery)
G. 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)
H. 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 5 years of age or older
B. Member has moderate to severe pruritus and drug-induced pruritus has been ruled out
C. Member has a confirmed molecular diagnosis of PFIC type 1, 2, or 3
   Note: Gene mutations associated with PFIC include the *ATP8B1* gene, *ABCB11* gene and *ABCB4* gene.
D. Member has serum bile acid level ≥ 100 μmol/L
E. 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)
F. Member has not received a liver transplant or surgical interruption of the enterohepatic circulation (e.g., partial external biliary diversion surgery)
G. 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)
H. Member experienced an inadequate treatment response or intolerance to Bylvay (odevixibat)
I. 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.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for all members (including new members) requesting continuation of therapy when the member is experiencing benefit from therapy (e.g., improvement in pruritis and reduction in serum bile acid). 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.

VI. 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.

VII. 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. Updated October 20, 2017. Accessed October 18, 2021.
4. National Organization for Rare Disorders (NORD). Alagille syndrome. Rare Disease Database. https://rarediseases.org. Published 2020. Accessed October 18, 2021.