Clinical Policy: Maralixibat (Livmarli)

Reference Number: ERX.SPA.442
Effective Date: 09.29.21
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Maralixibat (Livmarli™) is an ilieal bile acid transporter inhibitor.

FDA Approved Indication(s)
Livmarli is indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Livmarli is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Alagille Syndrome (must meet all)**:**

1. Diagnosis of ALGS-associated pruritus confirmed by one of the following (a or b):
   a. Genetic confirmation with presence of a mutation in *JAG1* or *NOTCH2;*
   b. Clinical confirmation of both of the following (i and ii):
      i. Bile duct paucity on liver biopsy;
      ii. Criteria meeting ≥ 3 of the 5 major criteria (*see Appendix D*);
2. Prescribed by or in consultation with hepatologist or gastroenterologist;
3. Age ≥ 12 months and ≤ 18 years at therapy initiation;
4. Pruritus requiring at least medium scratching (e.g., ≥ 2 on 0-4 scale);
5. Evidence of cholestasis that is met by ≥ 1 of the following (a – e):
   a. Total serum bile acid > 3 times upper limit of normal (ULN) for age;
   b. Conjugated bilirubin > 1 mg/dL;
   c. Fat-soluble vitamin deficiency otherwise unexplainable;
   d. Gamma-glutamyl transferase > 3 times ULN for age;
   e. Intractable pruritus explainable only by liver disease;
6. Failure of ursodeoxycholic acid, unless clinically significant adverse effects are experienced or contraindicated;
   **Prior authorization may be required for ursodeoxycholic acid*
7. Failure of an agent used for symptomatic relief of pruritus (e.g., antihistamine, rifampicin, cholestyramine), unless clinically significant adverse effects are experienced or all are contraindicated;
8. Documentation of member's current weight in kilograms;
9. Dose does not exceed 380 mcg/kg per day, up to a maximum of 28.5 mg (1 bottle) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Alagille Syndrome (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by an improvement in pruritus;
3. Documentation of member's current weight in kilograms;
4. If request is for a dose increase, new dose does not exceed 380 mcg/kg per day, up to a maximum 28.5 mg (1 bottle) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ALGS: Alagille syndrome
FDA: Food and Drug Administration
ULN: upper limit of normal

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ursodeoxycholic acid (Ursodiol®)*	10-30 mg/kg/day PO	N/A
rifampin (Rifadin®)	10 mg/kg PO	10 mg/kg/day
cholestyramine	4-16 g/day PO in 2 divided doses	16 g/day
antihistamine	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: Classic Criteria, Based on Five Body Systems, for a Diagnosis of ALGS

Classic Criteria	Description
Liver/cholestasis	Usually presenting as jaundice with conjugated hyperbilirubinaemia in the neonatal period, often with pale stools
Dysmorphic facies	Broad forehead, deep-set eyes, sometimes with upslanting palpebral fissures, prominent ears, straight nose with bulbous tip, and pointed chin giving the face a somewhat triangular appearance
Heart disease	Most frequently peripheral pulmonary artery stenosis, but also pulmonary atresia, atrial septal defect, ventricular septal defect, and Tetralogy of Fallot

Classic Criteria	Description
Axial skeleton/vertebral anomalies	Characteristic 'butterfly' vertebrae may be seen on an antero-posterior radiograph, and occasionally hemivertebrae, fusion of adjacent vertebrae, and spina bifida occulta
Eye/posterior embryotoxin	Anterior chamber defects, most commonly posterior embryotoxon, which is prominence of Schwalbe's ring at the junction of the iris and cornea

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>ALGS</td><td>Starting dose: 190 mcg/kg/day
Maintenance: 380 mcg/kg/day

<table>
<tr><th colspan="5">Individual dose volume by patient weight</th></tr>
<tr><th rowspan="2">Patient Weight (kg)</th><th colspan="2">Days 1-7 (190 mcg/kg once daily)</th><th colspan="2">Beginning Day 8 (380 mcg/kg once daily)</th></tr>
<tr><th>Volume QD (mL)</th><th>Dosing dispenser size (mL)</th><th>Volume QD (mL)</th><th>Dosing dispenser size (mL)</th></tr>
<tr><td>5-6</td><td>0.1</td><td rowspan="7">0.5</td><td>0.2</td><td rowspan="3">0.5</td></tr>
<tr><td>7-9</td><td>0.15</td><td>0.3</td></tr>
<tr><td>10-12</td><td>0.2</td><td>0.45</td></tr>
<tr><td>13-15</td><td>0.3</td><td>0.6</td><td rowspan="4">1</td></tr>
<tr><td>16-19</td><td>0.35</td><td>0.7</td></tr>
<tr><td>20-24</td><td>0.45</td><td>0.9</td></tr>
<tr><td>25-29</td><td>0.5</td><td>1</td></tr>
<tr><td>30-34</td><td>0.6</td><td rowspan="4">1</td><td>1.25</td><td rowspan="5">3</td></tr>
<tr><td>35-39</td><td>0.7</td><td>1.5</td></tr>
<tr><td>40-49</td><td>0.9</td><td>1.75</td></tr>
<tr><td>50-59</td><td>1</td><td>2.25</td></tr>
<tr><td>60-69</td><td>1.25</td><td rowspan="2">3</td><td>2.5</td></tr>
<tr><td>70 or higher</td><td>1.5</td><td>3</td></tr>
</table>
</td><td>380 mcg/kg/day, up to a maximum of 28.5 mg/day</td></tr>
</table>

VI. Product Availability

Oral solution: 9.5 mg/mL (30mL bottle)

VII. References

1. Livmarli Prescribing Information. Foster City, CA: Mirum Pharmaceuticals, Inc.; September 2021. Available at: https://files.mirumpharma.com/livmarli/livmarli-prescribinginformation.pdf. Accessed October 6, 2021.
2. Safety and efficacy study of LUM001 with a drug withdrawal period in participants with Alagille Syndrome (ALGS) (ICONIC). ClinicalTrials.gov Identifier: NCT02160782. Available at: https://clinicaltrials.gov/ct2/show/NCT02160782. Accessed May 21, 2021.
3. Kamath BM, Baker A, Houwen R, et al. Systematic review: the epidemiology, natural history, and burden of Alagille Syndrome. J Pediatr Gastroenterol Nutr 2018 Aug;67(2):148-156.
4. Turnpenny PD and Ellard S. Alagille syndrome: pathogenesis, diagnosis and management. Eur J Hum Genet. 2012 Mar; 20(3): 251–257.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	06.08.21	08.21
Drug is now FDA approved - criteria updated per FDA labeling: added maximum daily dose per PI; added requirement for documentation of member's weight in kg; references reviewed and updated.	10.12.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.