COMMON GROUND
HEALTHCARE COOPERATIVE

PHARMACY POLICY STATEMENT
Common Ground Healthcare Cooperative (CGHC)

DRUG NAME	**Livmarli (maralixibat)**
BENEFIT TYPE	Pharmacy
Coverage Requirements	Prior Authorization Required

Livmarli, approved by the FDA in 2021, is an ileal bile acid transport (IBAT) inhibitor indicated for the treatment of cholestatic pruritus in patients with Alagille Syndrome (ALGS) or progressive familial intrahepatic cholestasis (PFIC).
In cholestatic liver disease, biliary substances aren't eliminated from the liver, thus they re-enter circulation. Cholestatic itch is thought to be related to the accumulation of bile acids in the skin. Inhibiting IBAT decreases reuptake of bile salts to reduce serum bile acids and pruritis.
ALGS is a rare genetic disorder that can affect multiple organ systems, most commonly the liver, with a paucity of interlobular ducts.
PFIC is an ultra-rare group of genetic disorders that disrupt bile formation in the liver. It usually presents during infancy with cholestasis, jaundice, and intense itching. Most patients will eventually require biliary diversion surgery or liver transplant. PFIC1 involves extrahepatic manifestations while PFIC2 does not. However, PFIC2 can be complicated by hepatocellular carcinoma.

Livmarli (maralixibat) will be considered for coverage when the following criteria are met:

Alagille Syndrome (ALGS)

For **initial** authorization:
1. Member is at least 3 months of age; AND
2. Medication must be prescribed by or in consultation with a gastroenterologist OR hepatologist; AND
3. Member has a diagnosis of Alagille syndrome (ALGS) confirmed by the involvement of at least 3 of the following major clinical features:
   a) Hepatic Features (e.g., hyperbilirubinemia or scleral icterus)
   b) Cardiac Features (e.g., lesions confirmed on imaging or murmur)
   c) Facial Features (e.g., inverted triangular face, straight nose with bulbous tip)
   d) Ocular Features (e.g., embryotoxon, optic disk drusen)
   e) Skeletal Features (e.g., vertebral anomalies, osteopenia
   f) Renal Features (e.g., renal dysplasia, renal tubular acidosis)
   g) Vascular Features (e.g., narrowing of internal carotid artery, moyamoya disease)

NOTE: Member also meets criterion if has one or more clinical features and an affected first-degree relative; AND
4. Member must have liver biopsy demonstrating reduced number of the interlobular bile ducts OR confirmed finding of JAG1 or NOTCH2 gene mutation; AND
5. Member has symptoms of moderate to severe pruritus; AND
6. Member does NOT have any of the following:

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a) Previous liver transplant
b) Previous surgical disruption of enterohepatic circulation (partial external bile diversion or ileal exclusion)
c) Prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy)
d) History or presence of other concomitant liver disease

7. Member must have a trial and failure of at least 2 of the following:
   a) Cholestyramine
   b) Ursodiol
   c) Rifampin
   d) Naltrexone
8. **Dosage allowed/Quantity limit:** Starting dose is 190mcg/kg orally once daily, titrating up to 380 mcg/kg once daily. Max dose 28.5 mg (3 mL) per day.
   QL: 3 bottles (90 mL) per 30 days.
   Note: Use the 9.5 mg/mL oral solution for treatment of ALGS.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Pruritis has improved in response to therapy with Livmarli; AND
2. Member has not had a hepatic decompensation event.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Progressive Familial Intrahepatic Cholestasis (PFIC)

For **initial** authorization:
1. Member is at least 12 months of age; AND
2. Medication must be prescribed by or in consultation with a gastroenterologist OR hepatologist; AND
3. Member has a diagnosis of PFIC confirmed by genetic testing results: PFIC 1 (ATP8B1 mutation), PFIC2 (ABCB11 mutation), PFIC3 (ABCB4 mutation), PFIC4 (TJP2 mutation), or PFIC6 (MYO5B mutation); AND
4. Member has significant pruritis not attributed to another cause; AND
5. Documentation of total serum bile acid (sBA) ≥3× ULN; AND
6. Documentation of baseline liver function tests (e.g., ALT, AST, bilirubin, INR); AND
7. Trial and failure of ursodiol (may also continue concurrently); AND
8. Member does NOT have any of the following:
   a) Variants of the ABCB11 gene (PFIC type 2) that code for non-functional or complete absence of the bile salt export pump (BSEP-3) protein (per submitted genetic test result)
   b) Prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy)
   c) Liver transplant.
9. **Dosage allowed/Quantity limit:** Starting dose is 285 mcg/kg orally once daily, titrating up to recommended dose of 570 mcg/kg twice daily. Max dose 38 mg (2 mL) per day.
   QL: 2 bottles (60 mL) per 30 days.
   Note: Use the 19 mg/mL oral solution for treatment of PFIC.

If all the above requirements are met, the medication will be approved for 6 months.

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For **reauthorization**:
1. Pruritis has improved in response to therapy with Livmarli; AND
2. Member has not had a hepatic decompensation event.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Livmarli (maralixibat) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
10/15/2021	New policy for Livmarli created.
03/28/2023	Updated/added references. Changed lower age limit from 1 year to 3 months per updated drug label. Added QL. Added naltrexone to list of trial options and removed specific trial duration.
03/28/2024	Added criteria for new PFIC indication. Expanded description of hepatic decompensation contraindication in ALGS section (to match label).
08/02/2024	Added note about strengths to dosing sections. Added no hepatic decompensation to renewal sections. ALGS: Added note to diagnostic features criterion. PFIC: Changed at least 5 years of age to at least 12 months of age (label update); updated max qty.

References:

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