Clinical Policy Title:	Maralixibat
Policy Number:	RxA.709
Drug(s) Applied:	Livmarli®
Original Policy Date:	12/07/2021
Last Review Date:	10/19/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Cholestatic pruritus in patients with Alagille syndrome (ALGS) (must meet all):

1. Diagnosis of ALGS-associated pruritis confirmed by presence of the JAG1 or Notch2 gene mutation;
2. Prescribed by in consultation with a hepatologist or a gastroenterologist;
3. Age ≥ 3 months and ≤ 18 years of age at therapy initiation;
4. Symptoms of moderate to severe pruritus;
5. Cholestasis, as indicated by at least one (1) of the following:
   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 that is otherwise unexplainable;
   d. Gamma Glutamyl Transferase (GGT) > 3 times ULN for age;
   e. Intractable pruritus explainable only by liver disease;
6. Trial and failure of at least two (2) of the following medications used to treat pruritus, unless contraindicated or clinically significant adverse effects are experienced:
   a. Ursodiol (ursodeoxycholic acid);
   b. Bile acid sequestrants (e.g., Questran, Colestid, Welchol, cholestyramine);
   c. Rifampin;
7. Documentation of member's current weight in kilograms;
8. Requested dose does not exceed 380 mcg/kg per day up to a maximum of 28.5 mg (3 ml) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Cholestatic pruritus in patients with Alagille syndrome (ALGS) (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed new dose does not exceed 380 mcg/kg per day, up to a maximum 28.5 mg (3 mL) per day;

Approval Duration
Commercial: 12 months
Medicaid: 12 months

References

1. Mirum Pharmaceuticals, Inc. Long-Term, Open-Label Study with a Double-Blind, Placebo-Controlled, Randomized Drug Withdrawal Period of Lum001 (Maralixibat), an Apical Sodium-Dependent Bile Acid Transporter Inhibitor (Asbti), in Patients with Alagille Syndrome. clinicaltrials.gov; 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT02160782. Accessed June 5, 2023.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	10/19/2021	12/07/2021
Policy was reviewed: 1. Initial Approval Criteria, I.A.1: Updated diagnostic criteria from Diagnosis of cholestatic pruritus in patients with Alagille syndrome (ALGS) to Diagnosis of ALGS-associated pruritis with molecular genetic testing confirmed mutations in the JAG1 or NOTCH2 gene. 2. Initial Approval Criteria, I.A.6: Updated to remove prior disease criteria "Patient does not have chronic diarrhea requiring ongoing intravenous fluid or nutritional intervention". 3. Initial Approval Criteria, I.A.7: Updated to remove prior surgery criteria "No history of surgical interruption of enterohepatic circulation (for example, partial external biliary diversion [PEBD] surgery)". 4. Initial Approval Criteria, I.A.8: Updated to remove prior disease criteria "No clinical evidence of decompensated cirrhosis". 5. Initial Approval Criteria, I.A.6.b: Updated trial and failure criteria: Cholestyramine to Bile acid sequestrants (e.g., Questran, Colestid, Welchol, cholestyramine). 6. Initial Approval Criteria, I.A.6.d: Updated to remove prior trial and failure criteria	9/6/2022	10/19/2022

"Naltrexone". 7. Initial Approval Criteria, I.A.6.e: Updated to remove prior trial and failure criteria "Sertraline". 8. Initial Approval Criteria, I.A.6.d: Updated to include new trial and failure criteria Antihistamines (e.g., diphenhydramine, hydroxyzine). 9. Initial Approval Criteria, I.A.7: Updated to include new diagnostic criteria Documentation of member's current weight in kilograms. 10. Initial Approval Criteria, I.A: Updated approval duration criteria from 6 months to 12 months. 11. Continued Therapy Approval Criteria, II.A.3: Updated to include new diagnostic criteria Documentation of member's current weight in kilograms. 12. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.1: Updated diagnostic criteria from Diagnosis of ALGS-associated pruritis with molecular genetic testing confirmed mutations in the JAG1 or NOTCH2 gene to Diagnosis of ALGS-associated pruritis confirmed by presence of the JAG1 or Notch2 gene mutation. 2. Initial Approval Criteria, I.A.3: Updated age criteria from Age ≥ 1 years to Age ≥ 3 months and ≤ 18 years at therapy initiation. 3. Initial Approval Criteria, I.A.4: Updated diagnostic criteria from Symptoms of moderate to very severe pruritus to	06/05/2023	07/13/2023

Symptoms of moderate to severe pruritus. 4. Initial Approval Criteria, I.A.6.d: Updated trial and failure criteria to remove “Antihistamines (e.g., diphenhydramine, hydroxyzine)”. 5. Continued Therapy Approval Criteria, II.A.2: Updated diagnostic criteria from Member is responding positively to therapy; (eg tolerating therapy and documentation of improvement in pruritis); to Member is responding positively to therapy 6. Continued Therapy Approval Criteria, II.A.3: Updated to remove prior documentation criteria "Documentation of member’s current weight in kilograms" 7. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023