Effective Date: 04/01/2022
Reviewed: 01/2022, 01/2023, 05/2023, 8/2023, 01/2024 Scope: Medicaid

SPECIALTY GUIDELINE MANAGEMENT

BYLVAY (odevixibat)

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 Indications

A. Bylvay is indicated for the treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC).

Limitations of Use: Bylvay may not be effective in PFIC type 2 patients with specific ABCB11 variants resulting in nonfunctional or complete absence of bile salt export pump protein (BSEP-3).

B. Bylvay is indicated for the treatment of cholestatic pruritus in patients 12 months of age and older with Alagille syndrome (ALGS).

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 and genetic testing results confirming a diagnosis of progressive familial intrahepatic cholestasis (PFIC) type 1, 2, or 3 or Alagille syndrome (ALGS) 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. EXCLUSIONS

Coverage will not be provided for members who have PFIC type 2 with variants in the ABCB11 gene that predict non-functional or complete absence of bile salt export pump protein (BSEP-3).

IV. PRESCRIBER SPECIALTIES

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

V. CRITERIA FOR INITIAL APPROVAL

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 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 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, biliary atresia, benign recurrent intrahepatic cholestasis [BRIC], liver cancer, alternate non-PFIC related etiology of cholestasis) 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's dose will not exceed 40 mcg/kg/day. Member's current weight and prescribed dose must be provided.

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 12 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:
   i. Genetic testing (i.e., presence of mutation in the *JAG1* or *NOTCH2* gene)
   ii. Member has both of the following:
      a. Bile duct paucity
      b. Three of the five major clinical features of ALGS:
         1. Cholestasis
         2. Cardiac defect (e.g., stenosis of the peripheral pulmonary artery and its branches)
         3. Skeletal abnormality (e.g., butterfly vertebrae)
         4. Ophthalmologic abnormality (e.g., posterior embryotoxon)
         5. 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:
   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
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, intolerance or contraindication 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 experienced an inadequate treatment response, intolerance, or contraindication to Livmarli (maralixibat)
I. Member's dose will not exceed 120 mcg/kg/day. Member's current weight and prescribed dose must be provided

VI. 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 120 mcg/kg/day and if requesting dose increase for PFIC, documentation supports no improvement in pruritus after at least 3 months at each dose of 40 mcg/kg/day and 80 mcg/kg/day, if applicable.

VII. QUANTITY LIMIT

A. Bylvay oral pellets 200 mcg – 360 per 30 days, daily dose of 12
B. Bylvay oral pellets 600 mcg – 120 per 30 days, daily dose of 4
C. Bylvay capsules 400 mcg – 540 per 30 days, daily dose of 18
D. Bylvay capsules 1200 mcg – 180 per 30 days, daily dose of 6

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>PFIC</td><td>The recommended dosage of Bylvay is 40 mcg/kg once daily in the morning with a meal. If there is no improvement in pruritus after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once daily, not to exceed a total daily dose of 6 mg.

Bylvay oral pellets are intended for use by patients weighing < 19.5 kg, while Bylvay capsules are intended for use by patients weighing ≥ 19.5 kg.

The table below shows the recommended weight-based total daily dosage needed for the
<table>
<tr><th>Body Weight (kg)</th><th>Total Daily Dose (mcg)</th></tr>
<tr><td>≤ 7.4</td><td>200</td></tr>
<tr><td>7.5 – 12.4</td><td>400</td></tr>
<tr><td>12.5 – 17.4</td><td>600</td></tr>
<tr><td>17.5 – 25.4</td><td>800</td></tr>
<tr><td>25.5 – 35.4</td><td>1200</td></tr>
<tr><td>35.5 – 45.4</td><td>1600</td></tr>
<tr><td>45.5 – 55.4</td><td>2000</td></tr>
<tr><td>≥55.5</td><td>2400</td></tr>
</table>
recommended dosage at 40 mcg/kg once daily.</td><td>6 mg/day</td></tr>
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<table>
<tr>
<td>ALGS</td>
<td>The recommended dosage of Bylvay is 120 mcg/kg once daily in the morning with a meal.

The table below shows the recommended weight-based total daily dosage needed for the recommended dosage at 120 mcg/kg once daily.

<table>
<tr><th>Body Weight (kg)</th><th>Total Daily Dose (mcg)</th></tr>
<tr><td>≤ 7.4</td><td>600</td></tr>
<tr><td>7.5 – 12.4</td><td>1200</td></tr>
<tr><td>12.5 – 17.4</td><td>1800</td></tr>
<tr><td>17.5 – 25.4</td><td>2400</td></tr>
<tr><td>25.5 – 35.4</td><td>3600</td></tr>
<tr><td>35.5 – 45.4</td><td>4800</td></tr>
<tr><td>45.5 – 55.4</td><td>6000</td></tr>
<tr><td>≥55.5</td><td>7200</td></tr>
</table>
</td>
<td>120mcg/kg/day</td>
</tr>
</table>

VIII. REFERENCES

1. Bylvay [package insert]. Boston, MA: Albireo Pharma, Inc.; June 2023.