Pharmacy Policy Bulletin: J-1111 Bylvay (odevixibat) – Commercial and Healthcare Reform	
Number: J-1111	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1111-006	**Original Date:** 10/06/2021
Effective Date: 10/28/2024	**Review Date:** 10/02/2024

Drugs Product(s):	• Bylvay (odevixibat)
FDA-Approved Indication(s):	• Treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC) • Treatment of cholestatic pruritus in patients 12 months of age and older with Alagille syndrome (ALGS)

Background:	• Bylvay is an oral ileal bile acid transporter inhibitor. Bylvay decreases the reabsorption of bile acids from the terminal ileum by acting as a reversible inhibitor of the ileal bile acid transporter. The complete mechanism by which Bylvay improves pruritis in PFIC and ALGS patients is unknown, but it may be due to a decrease in serum bile acids which is thought to be the cause of pruritis in PFIC and ALGS patients. • PFIC is a rare, autosomal recessive, genetic disorder caused by a buildup of bile in liver cells leading to progressive liver disease and liver failure. The main clinical features of PFIC include cholestasis, jaundice, and pruritis, with symptoms typically appearing in infancy or early childhood. • There are three classic types of PFIC. Bylvay was only evaluated in patients with PFIC types 1 or 2. PFIC types 1 and 2 are characterized by low γ-glutamyltranspeptidase, severe pruritus and various extrahepatic manifestations. PFIC type 1 is caused by mutations in the ATP8B1 gene (F1C1) and PFIC type 2 is caused by mutations in the ABCB11 gene (BSEP). • No medical therapy of proven benefit for long-term prognosis of PFIC exists. Liver transplantation is the recommended treatment of end-stage disease in PFIC. • ALGS is a rare, autosomal dominant multisystem disorder associated with disrupted Notch signaling, which leads to the abnormal development of the intrahepatic bile ducts. The predominating liver-related clinical features of ALGS are chronic cholestasis, jaundice, and cirrhosis with symptoms typically developing around 3 months of life.

	• Pruritus has been shown to affect 59%–88% of ALGS patients, with up to 45% reporting severe pruritus. This unrelenting itching is associated with additional symptoms, such as skin damage, sleep problems, mood disturbances, and reduced health-related quality of life. One-third of parents recognized itching as the characteristic of ALGS that affected their children most. • 92% of patients in the ALGS clinical trial for Bylvay had the JAGGED1 (JAG1) mutation; 8% of patients had the NOTCH2 mutation. • Bylvay reduces serum bile acids in patients with PFIC and ALGS. Normal serum bile acids are generally ≤ 10 µmol/L, depending on laboratory reference range. • Bylvay was not evaluated in PFIC or ALGS patients with cirrhosis. Patients should be closely monitored for liver test abnormalities. Bylvay should be permanently discontinued if a patient progresses to portal hypertension or experiences a hepatic decompensation event. • In clinical studies, the efficacy of Bylvay for pruritis was evaluated at 24 weeks. Additionally, serum bile acid concentrations were reduced from baseline within 4-8 weeks of treatment with Bylvay. • ICD-10 Code Information: ○ ICD-10 codes K76.8 (other specified diseases of liver) and E78.7 (disorder of bile acid and cholesterol metabolism, unspecified) may apply to Bylvay; however, the prescriber must confirm the patient has PFIC. ○ ICD-10: Q44.7 “Congenital malformations of gallbladder, bile ducts and liver” may apply to Alagille syndrome; however, the prescriber must specify the diagnosis ○ ICD-10: L29.9 “Pruritus, unspecified” may apply to cholestatic pruritus associated with Alagille syndrome; however, the prescriber must specify the diagnosis • Prescribing Considerations: ○ Bylvay should be prescribed by or in consultation with a hepatologist, gastroenterologist, or provider specialized in treating PFIC or ALGS. ○ Baseline liver tests and fat-soluble vitamin levels should be obtained and monitored during treatment. ○ Bylvay may cause dehydration, diarrhea, abdominal pain, and vomiting. ○ Capsules should not be crushed or chewed and may be mixed into soft food or liquid. Pellets should not be swallowed whole and should be mixed with food or liquid. ○ Bylvay should be administered at least 4 hours before or 4 hours after administering a bile acid binding resin. ○ Bylvay may not be effective in PFIC type 2 patients with ABCB11 variants resulting in non-functional or complete absence of bile acid binding resin.

Approval Criteria

I. Initial Authorization

A. PFIC

When a benefit, coverage of Bylvay may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member is 3 months of age or older.

2. The member has a diagnosis of one (1) of the following confirmed by genetic testing **(a. or b.)**:

a. PFIC type 1

b. PFIC type 2 with bile salt export pump protein (BSEP-3) function

3. The member has a diagnosis of pruritis (ICD-10: L29.8, L29.9).

4. The member has elevated serum bile acids above the laboratory reference range.

5. The member does not have cirrhosis, portal hypertension, or history of hepatic decompensation.

B. ALGS

When a benefit, coverage of Bylvay may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member is 12 months of age or older.
2. The member has a diagnosis of Alagille syndrome (no ICD-10 code) confirmed by genetic testing demonstrating a *JAGGED1* or *NOTCH2* deletion or mutation.
3. The member has elevated serum bile acid levels above the laboratory reference range.
4. The provider attests that the member experiences cholestatic pruritus explained only by liver disease.
5. The member does not have cirrhosis, portal hypertension, or history of hepatic decompensation.

II. Reauthorization

When a benefit, reauthorization of Bylvay may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member has experienced improvement in pruritis.
B. The member has experienced a decrease in serum bile acids from baseline.
C. The prescriber attests that the member has not progressed to cirrhosis, portal hypertension, or hepatic decompensation.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization

- Commercial and HCR Plans: If approved, up to a 6 month authorization may be granted.
  - Note: For Delaware Commercial fully-insured and ACA members, a 12 month authorization must be granted pursuant to 18 *Del. C.* §§3376(a) and 3586(a) and market conduct examination docket #5467 (Exam Authority #53287-22-701).

Reauthorization

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

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

2. ClinicalTrials.gov. NCT03566238. Available at: https://clinicaltrials.gov/ct2/show/NCT03566238?term=NCT03566238&draw=2&rank=1. Accessed June 26, 2024.
3. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of cholestatic liver diseases. *Journal of Hepatology* 51 (2009) 237–267.
4. Amirneni S, Haep N, Gad M, et al. Molecular overview of progressive familial intrahepatic cholestasis. *World J Gastroenterol* 2020 December 21; 26(47): 7470-7484.
5. Mayo Clinic Laboratories. Test IS: BILEA. Available at: https://www.mayocliniclabs.com/test-catalog/Clinical+and+Interpretive/84689. Accessed June 26, 2024.
6. Gunaydin M, Bozkurter Cil AT. Progressive familial intrahepatic cholestasis: diagnosis, management, and treatment. *Hepat Med*. 2018;10:95-104.
7. van der Woerd WL, Houwen RH, van de Graaf SF. Current and future therapies for inherited cholestatic liver diseases. *World J Gastroenterol*. 2017;23(5):763-775.
8. Cies JJ, Giamalis JN. Treatment of cholestatic pruritus in children. *Am J Health Syst Pharm*. 2007;64(11):1157-1162.
9. Kamath BM, Baker A, Houwen R, et al. Systematic review: the epidemiology, natural history, and burden of Alagille syndrome. *J Pediatr Gastroenterol Nutr*. 2018;67(2):148-156.
10. Ameur SB, Chabchoub I, Telmoudi J, et al. Management of cholestatic pruritus in children with Alagille syndrome: case report and literature review. *Arch Pediatr*. 2016;23(12):1247-1250.
11. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of Cholestatic Liver Diseases. *Journal of Hepatology*. 2009(51):237–267.
12. Pollock G, Minuk GY. Diagnostic considerations for cholestatic liver disease. *J Gastroenterol Hepatol*. 2017;32(7):1303-1309.
13. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on genetic cholestatic liver diseases. *Journal of Hepatology* (2024) 1–23. Available at: EASL Clinical Practice Guidelines on genetic cholestatic liver diseases (journal-of-hepatology.eu). Accessed July 3, 2024.