PRIOR AUTHORIZATION POLICY

POLICY: Hepatology – Bylvay Prior Authorization Policy
- Bylvay™ (odevixibat capsules and oral pellets – Albireo Pharma)

REVIEW DATE: 07/24/2024

OVERVIEW

Bylvay, an ileal bile acid transporter (IBAT) inhibitor, is indicated for the treatment of:
- Pruritus in patients ≥ 3 months of age with **progressive familial intrahepatic cholestasis** (PFIC).[1]
- Cholestatic pruritus in patients ≥ 12 months of age with **Alagille syndrome** (ALGS).[1]

Disease Overview

PFIC is a group of rare, autosomal recessive liver diseases defined by genetic mutations affecting bile acid transporters (e.g., mutation of the *ATP8B1* gene, *ABCB11* gene, *ABCB4* gene, *TJP2* gene, *NR1H4* gene, and *MYO5B* gene).[2-4] **ALGS** is a rare liver disease defined by genetic deletion or mutation affecting bile acid transporters (e.g., deletion or mutation of the *JAG1* gene or *NOTCH2* gene).[5,8,9] Progression of both diseases can cause liver fibrosis, cirrhosis, or end-stage liver disease and leads to death at an early age in life (infancy to adolescence).

Cholestasis, jaundice, and pruritus are common symptoms in patients with PFIC and ALGS.[8,9] Although the complete mechanism by which Bylvay improves pruritus in these patients is unknown, it may involve inhibition of the IBAT, which results in decreased reuptake of bile salts, as observed by a decrease in serum bile acids. Cholestyramine, rifampicin, and ursodeoxycholic acid (ursodiol) have been used off-label for decades to alleviate symptoms related to PFIC and ALGS.[5,6,9] Cholestyramine, ursodeoxycholic acid, rifampicin, naltrexone, and sertraline are recommended in clinical practice guidelines from the European Association for the Study of the Liver (2009).[7]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Bylvay. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Bylvay as well as the monitoring required for adverse events and long-term efficacy, approval requires Bylvay to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Bylvay is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Progressive Familial Intrahepatic Cholestasis**. Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi and vii):

i. Patient is ≥ 3 months of age; AND
ii. Patient has moderate-to-severe pruritus, according to the prescriber; AND
iii. Diagnosis of progressive familial intrahepatic cholestasis was confirmed by genetic testing demonstrating a gene mutation affiliated with progressive familial intrahepatic cholestasis; AND
Note: Gene mutations affiliated with progressive familial intrahepatic cholestasis include the *ATP8B1* gene, *ABCB11* gene, *ABCB4* gene, *TJP2* gene, *NR1H4* gene, and *MYO5B* gene.
iv. Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory; AND
v. Patient has tried at least two systemic medications for progressive familial intrahepatic cholestasis, unless contraindicated; AND
Note: Systemic medications for progressive familial intrahepatic cholestasis include cholestyramine, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol).
vi. Patient does not have any of the following (a, b, or c):
a) Cirrhosis; OR
b) Portal hypertension; OR
c) History of a hepatic decompensation event; AND
Note: Examples of a hepatic decompensation event include variceal hemorrhage, ascites, and hepatic encephalopathy.
vii. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in progressive familial intrahepatic cholestasis.

B) Patient is Currently Receiving Bylvay. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
i. Patient does not have any of the following (a, b, or c):
a) Cirrhosis; OR
b) Portal hypertension; OR
c) History of a hepatic decompensation event; AND
Note: Examples of a hepatic decompensation event include variceal hemorrhage, ascites, and hepatic encephalopathy.
ii. Patient had response to therapy, as determined by the prescriber; AND
Note: Examples of response to therapy include decrease in serum bile acids and decrease in pruritus.
iii. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in progressive familial intrahepatic cholestasis.

2. Alagille Syndrome. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi and vii):
i. Patient is ≥ 12 months of age; AND
ii. Patient has moderate-to-severe pruritus, according to the prescriber; AND
iii. Diagnosis of Alagille syndrome was confirmed by genetic testing demonstrating a *JAG1* or *NOTCH2* deletion or mutation; AND
iv. Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory; AND
v. Patient has tried at least two systemic medications for Alagille syndrome, unless contraindicated; AND
Note: Systemic medications for Alagille syndrome include cholestyramine, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol).
vi. Patient does not have any of the following (a, b, or c):
a) Cirrhosis; OR

b) Portal hypertension; OR
c) History of a hepatic decompensation event; AND
Note: Examples of a hepatic decompensation event include variceal hemorrhage, ascites, and hepatic encephalopathy.

vii. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in Alagille syndrome.

C) Patient is Currently Receiving Bylvay. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient does not have any of the following (a, b, or c):
a) Cirrhosis; OR
b) Portal hypertension; OR
c) of a hepatic decompensation event; AND
Note: Examples of a hepatic decompensation event include variceal hemorrhage, ascites, and hepatic encephalopathy.

ii. Patient had response to therapy, as determined by the prescriber; AND
Note: Examples of response to therapy include decrease in serum bile acids and decrease in pruritus.

iii. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in Alagille syndrome.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Bylvay is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Bylvay™ capsules and oral pellets [prescribing information]. Boston, MA: Albireo Pharma; February 2024.
2. Davit-Spraul, A, Gonzales, E, Baussan, C, et al. Progressive familial intrahepatic cholestasis. *Orphanet J Rare Dis*. 2009;4:1.
3. Amirneni S, Haep N, Gad MA, et al. Molecular overview of progressive familial intrahepatic cholestasis. *World J Gastroenterol*. 2020 Dec 21;26(47):7470-7484.
4. Gunaydin M, Bozkurter Cil AT. Progressive familial intrahepatic cholestasis: diagnosis, management, and treatment. *Hepat Med*. 2018 Sep 10;10:95-104.
5. van der Woerd WL, Houwen RH, van de Graaf SF. Current and future therapies for inherited cholestatic liver diseases. *World J Gastroenterol*. 2017 Feb 7;23(5):763-775.
6. Gunaydin M, Bozkurter C. Progressive familial intrahepatic cholestasis: diagnosis, management, and treatment. *Hepat Med*. 2018 Sep 10;10:95-104.
7. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. *J Hepatol*. 2009 Aug;51(2):237-67.
8. Alagille syndrome. National Organization for Rare Disorders. Updated 2024. Available at: https://rarediseases.org/rare-diseases/alagille-syndrome/. Accessed on July 16, 2024.
9. Diaz-Frias J, Kondamudi NP. Alagille Syndrome. [Updated 2022 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507827/. Accessed on July 16, 2024.