# Drug Coverage Policy

**Effective Date ..... 11/1/2024**
**Coverage Policy Number.....IP0363**
**Policy Title.....Bylvay**

# Hepatology – Bylvay

- Bylvay™ (odevixibat capsules and oral pellets – Albireo Pharma)

***INSTRUCTIONS FOR USE***
*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

## Cigna Healthcare Coverage Policy

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]

## Medical Necessity Criteria

**Bylvay is considered medically necessary when ONE of the following is met:**

**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 pathogenic gene variant affiliated with progressive familial intrahepatic cholestasis; AND
       Note: Gene variants 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 pathogenic variant; 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)** 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 Alagille syndrome.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (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.

## Revision Details

| Type of Revision | Summary of Changes | Date |
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| Annual Revision | **Updated** policy name from "Odevixibat" from "Hepatology – Bylvay"<br><br>**Progressive Familial Intrahepatic Cholestasis**.<br>**Added** "Patient is Currently Receiving Bylvay" criteria<br>**Updated** "Has moderate-to-severe pruritus" to "Patient has moderate-to-severe pruritus, according to the prescriber"<br>**Updated** "Documentation of failure, contraindication, or intolerance to **TWO** systemic medications for progressive familial intrahepatic cholestasis (for example, cholestyramine, naltrexone, rifampicin, sertraline, or ursodeoxycholic acid [ursodiol])" to "Patient has tried at least two systemic medications for progressive familial intrahepatic cholestasis, unless contraindicated; Note: Systemic medications for progressive familial intrahepatic cholestasis include cholestyramine, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol)."<br>**Updated** "Diagnosis of progressive familial intrahepatic cholestasis was confirmed by genetic testing demonstrating a gene mutation affiliated with progressive familial intrahepatic cholestasis; Note: Gene mutations affiliated with progressive familial intrahepatic cholestasis include the *ATP8B1* gene, *ABCB11* gene, *ABCB4* gene, *TJP2* gene, | 11/1/2024 |

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| | *NR1H4* gene*,* and *MYO5B* gene" to "Diagnosis of progressive familial intrahepatic cholestasis was confirmed by genetic testing demonstrating a pathogenic gene variant affiliated with progressive familial intrahepatic cholestasis;<br>Note: Gene variants affiliated with progressive familial intrahepatic cholestasis include the *ATP8B1* gene*, ABCB11* gene*, ABCB4* gene*, TJP2* gene*, NR1H4* gene*,* and *MYO5B* gene."<br><br>**Alagille Syndrome**.<br>**Added** "Patient is Currently Receiving Bylvay" criteria<br>**Updated** "Has moderate-to-severe pruritus" to "Patient has moderate-to-severe pruritus, according to the prescriber"<br>**Updated** "Failure, contraindication, or intolerance to at least **TWO** systemic medications for Alagille syndrome, unless contraindicated (for example, cholestyramine, naltrexone, rifampicin, sertraline, or ursodeoxycholic acid [ursodiol])" to "Patient has tried at least two systemic medications for Alagille syndrome, unless contraindicated; Note: Systemic medications for Alagille syndrome include cholestyramine, naltrexone, rifampicin, sertraline, and ursodeoxycholic acid (ursodiol)"<br>**Updated** "Documented diagnosis of Alagille syndrome was confirmed by genetic testing demonstrating a *JAG1* or *NOTCH2* deletion or mutation" to "Documented diagnosis of Alagille syndrome was confirmed by genetic testing demonstrating a *JAG1* or *NOTCH2* deletion or pathogenic variant" | |

The policy effective date is in force until updated or retired.