**Effective Date** ..... 12/15/2023
**Next Review Date** ..... 12/15/2024
**Coverage Policy Number** ..... IP0363

# Odevixibat

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## Related Coverage Resources

***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. 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.*

## Overview

This policy supports medical necessity review for odevixibat capsules and oral pellets (**Bylvay**™).

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

## Medical Necessity Criteria

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

1. **Progressive Familial Intrahepatic Cholestasis.** Individual meets **ALL** of the following criteria:
   A. 3 months of age or older
   B. Has moderate-to-severe pruritus
   C. Documented diagnosis of progressive familial intrahepatic cholestasis confirmed by genetic testing demonstrating a gene mutation affiliated with progressive familial intrahepatic cholestasis (for example, *ATP8B1* gene, *ABCB11* gene, *ABCB4* gene, *TJP2* gene, *NR1H4* gene, *MYO5B* gene)

D. Has a serum bile acid concentration above the upper limits of the normal reference range for the reporting laboratory
E. 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])
F. Does not have any of the following:
    i. Cirrhosis
    ii. Portal hypertension
    iii. History of a hepatic decompensation event (for example, variceal hemorrhage, ascites, hepatic encephalopathy)
G. 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.** Individual meets **ALL** of the following criteria:
    A. 12 months of age or older
    B. Has moderate-to-severe pruritus
    C. Documented diagnosis of Alagille syndrome was confirmed by genetic testing demonstrating a *JAG1* or *NOTCH2* deletion or mutation
    D. Has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory
    E. 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])
    F. Does not have any of the following:
        i. Cirrhosis
        ii. Portal hypertension
        iii. History of a hepatic decompensation event (for example, variceal hemorrhage, ascites, and hepatic encephalopathy)
    G. 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.

## Reauthorization Criteria

**Continuation of odevixibat (Bylvay) is considered medically necessary for ALL covered diagnoses when ALL of the following are met:**

1. The above medical necessity criteria have been met prior to the start of Bylvay therapy
2. Does not have any of the following:
    A. Cirrhosis
    B. Portal hypertension
    C. History of a hepatic decompensation event (for example, variceal hemorrhage, ascites, and hepatic encephalopathy)
3. There is documentation of beneficial response since initiating Bylvay therapy compared with baseline
4. The medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in progressive familial intrahepatic cholestasis or Alagille syndrome.

## Authorization Duration

Initial approval duration: up to 6 months
Reauthorization approval duration: up to 12 months

## Conditions Not Covered

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

## Background

**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]

## References


1. Bylvay™ capsules and oral pellets [prescribing information]. Boston, MA: Albireo Pharma; June 2023.
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 2020. Available at: https://rarediseases.org/rare-diseases/alagille-syndrome/. Accessed on June 19, 2023.
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 June 19, 2023