UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 2251-7
Program	Prior Authorization/Medical Necessity
Medication	Bylvay™ (odevixibat)
P&T Approval Date	10/2021, 12/2021, 12/2022, 8/2023, 10/2023, 8/2024, 8/2025
Effective Date	11/1/2025

1. Background:

Bylvay (odevixibat) is an ileal bile acid transporter inhibitor indicated for the treatment of pruritis in patients aged 3 months or older with progressive familial intrahepatic cholestasis (PFIC). Bylvay is also indicated for the treatment of pruritis in patients 12 months of age and older with Alagille syndrome (ALGS).

PFIC is a heterogeneous group of liver disorders of autosomal recessive inheritance, characterized by an early onset of cholestasis (usually during infancy) with pruritus and malabsorption, which rapidly progresses and ends up as liver failure. Pruritus is the most obvious and the most unbearable symptom in cholestasis. It has been proposed that it is induced by the stimulation of nonmyelinated subepidermal free nerve ends because of increased serum bile acids.

ALGS is a rare genetic disorder caused by a mutation in the JAG1 or Notch2 genes which are involved in embryonic development in utero. In ALGS patients, multiple organ systems may be affected by the mutation. In the liver, the mutation causes the bile ducts to abnormally narrow, malform and reduce in number, leading to bile acid accumulation, cholestasis, and ultimately progressive liver disease. The cholestatic pruritus experienced by patients with ALGS is among the most severe in any chronic liver disease and is present in most affected children by the third year of life.

Conventional treatments for pruritis associated with PFIC or Alagille syndrome include uroseoxycholic acid (UCDA), antihistamines (e,g., diphenhydramine), bile acid sequestrants (e.g., cholestyramine), rifampin, naltrexone and sertraline.

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

2. Coverage Criteria[a]:

A. Progressive Familial Intrahepatic Cholestasis

1. **Initial Authorization**

   a. **Bylvay** will be approved based upon **all** of the following criteria:

      (1) Confirmed molecular diagnosis of progressive familial intrahepatic cholestasis (PFIC)

      -AND-

      (2) Patient does not have a ABCB11 variant resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3)

      -AND-

      (3) Patient is experiencing moderate to severe pruritus associated with PFIC.

      -AND-

      (4) Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory.

      -AND-

      (5) Patient has had an inadequate response to at least two other conventional treatments for the symptomatic relief of pruritus (e.g., uroseoxycholic acid, diphenhydramine, cholestyramine, rifampin, naltrexone, and sertraline).

      -AND-

      (6) Prescribed by a gastroenterologist or hepatologist.

      Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Bylvay** will be approved based on **both** of the following criteria:

      (1) Documentation of positive clinical response to Bylvay therapy (e.g., reduced serum bile acids, improved pruritis and less sleep disturbance)

      -AND-

      (2) Prescribed by a gastroenterologist or hepatologist.

      Authorization will be issued for 12 months.

B. Alagille Syndrome

1. **Initial Authorization**

   a. **Bylvay** will be approved based upon **all** of the following criteria:

      (1) Diagnosis of Alagille syndrome (ALGS)

      -AND-

      (2) Confirmation of diagnosis by presence of the JAG1 or Notch2 gene mutation

      -AND-

      (3) Patient has a serum bile acid concentration above the upper limit of the normal reference range for the reporting laboratory.

      -AND-

      (4) Patient is experiencing moderate to severe pruritis associated with ALGS

      -AND-

      (5) Patient has had an inadequate response to at least two other conventional treatments for the symptomatic relief of pruritus (e.g., ursodeoxycholic acid, diphenhydramine, cholestyramine, rifampin, naltrexone, and sertraline).

      -AND-

      (6) Prescribed by a gastroenterologist or hepatologist.

      Authorization will be issued for 12 months.

2. **Reauthorization**

   a. Bylvay will be approved based on **both** of the following criteria:

      (1) Documentation of positive clinical response to Bylvay therapy (e.g., reduced serum bile acids, improved pruritis)

      -AND-

      (2) Prescribed by a gastroenterologist or hepatologist.

      Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. Reference:

1. Bylvay [package insert]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; March 2025.
2. Thompson RJ, Arnell H, Artan R, et al. Odevixibat treatment in progressive familial intrahepatic cholestasis: a randomised, placebo-controlled, phase 3 trial. *Lancet Gastroenterol Hepatol*. 2022;7(9):830-842.
3. Ovchinsky N, Aumar M, Baker A, et al. Efficacy and safety of odevixibat in patients with Alagille syndrome (ASSERT): a phase 3, double-blind, randomised, placebo-controlled trial. *Lancet Gastroenterol Hepatol*. 2024;9(7):632-645.
4. Chowdhury JR, Chowdhury NR. Inherited disorders associated with conjugated hyperbilirubinemia in adults. In: Post TW, ed. *UpToDate*. UpToDate, 2025. Accessed June 23, 2025. Inherited disorders associated with conjugated hyperbilirubinemia in adults - UpToDate
5. Kohut TJ, Loomes KM. Alagille syndrome. In: Post TW, ed. *UpToDate.* UpToDate, 2025. Accessed June 23, 2025. Alagille syndrome - UpToDate

Program	Prior Authorization/Medical Necessity - Bylvay (odevixibat)
Change Control	
10/2021	New program
12/2021	Updated criteria with addition of elevated sBA level requirement.
12/2022	Annual review with no changes to coverage criteria. Updated references.
8/2023	Updated examples of conventional treatment for pruritus associated with PFIC. Added coverage criteria for new ALGS indication. Updated background and references.
10/2023	Removed requirement that PFIC must be type 1 or 2. Expanded prescriber requirement to include gastroenterologist.
8/2024	Annual review. Updated examples of conventional treatment and initial authorization durations. Updated background and references.
8/2025	Annual review with no changes to criteria. Updated references.