

**Clinical Policy: Odevixibat (Bylvay)**

Reference Number: CP.PHAR.528

Effective Date: 07.20.21

Last Review Date: 11.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Odevixibat (Bylvay™) is a non-systemic ileal bile acid transport inhibitor.

**FDA Approved Indication(s)**

Bylvay is indicated for the treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC).

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

**Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that Bylvay is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Progressive Familial Intrahepatic Cholestasis (must meet all):**

1. Diagnosis of genetically confirmed PFIC type 1 or 2 (formerly known as Byler disease or syndrome) with presence of both of the following (a and b):
  - a. Pruritus requiring at least medium scratching (e.g.,  $\geq 2$  on 0 to 4 scale);
  - b. Serum bile acids  $\geq 100$   $\mu\text{mol/L}$ ;
2. Prescribed by or in consultation with a hepatologist or gastroenterologist;
3. Age  $\geq 3$  months;
4. Member does not have pathologic variations of the ABCB11 gene that predict complete absence of the BSEP protein;
5. Failure of ursodeoxycholic acid, unless clinically significant adverse effects are experienced or contraindicated;
6. Failure of an agent used for symptomatic relief of pruritus (e.g., antihistamine, rifampicin, cholestyramine), unless clinically significant adverse effects are experienced or all are contraindicated;
7. Documentation of member's current weight in kg;
8. Dose does not exceed one of the following (a, b, or c):
  - a. 40 mcg/kg per day, not to exceed the recommended dose and quantity by body weight as outlined in Section V;

- b. 80 mcg/kg per day (up to a maximum of 6 mg per day), and documentation supports no improvement in pruritus after 3 months at a dose of 40 mcg/kg per day;
- c. 120 mcg/kg per day (up to a maximum of 6 mg per day), and documentation supports no improvement in pruritus after 3 months at a dose of 80 mcg/kg per day.

**Approval duration: 6 months**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Progressive Familial Intrahepatic Cholestasis (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters:
  - a. Improvement in pruritus;
  - b. Reduction of serum bile acids from baseline;
3. Documentation of member's current weight in kg;
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
  - a. 40 mcg/kg per day, not to exceed the recommended dose and quantity by body weight as outlined in Section V;
  - b. 80 mcg/kg per day (up to a maximum of 6 mg per day), and documentation supports no improvement in pruritus after 3 months at a dose of 40 mcg/kg per day;
  - c. 120 mcg/kg per day (up to a maximum of 6 mg per day), and documentation supports no improvement in pruritus after 3 months at a dose of 80 mcg/kg per day.

**Approval duration: 12 months**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.  
**Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

<p>ABCB11: ATP binding cassette subfamily B member 11</p> <p>BSEP-3: bile salt export pump 3</p> <p>FDA: Food and Drug Administration</p>	<p>IBAT: ileal bile acid transporter</p> <p>ObsRO: observer-reported outcome</p> <p>PFIC: progressive familial intrahepatic</p>
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*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ursodeoxycholic acid (Ursodiol <sup>®</sup> )*	15-30 mg/kg/day	30 mg/kg/day
Example of therapies for pruritus: antihistamine, rifampicin, cholestyramine	Varies	Varies

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*\*Off-label*

*Appendix C: Contraindications/Boxed Warnings*

None reported

*Appendix D: General Information*

- Initial care for patients with PFIC targets symptoms and nutritional problems, including fat-soluble vitamin supplementation.
- Off-label conventional treatment for PFIC pruritus includes antihistamines, rifampicin, and cholestyramine. In the pivotal PEDFIC 1 study, 85% of placebo and 57.1% of Bylvay patients were already receiving rifampicin.
- Ursodiol is usually considered first line therapy for all PFIC types and has been proven to improve liver function and pruritus. Use of Ursodiol is supported by expert opinion; additionally, in the pivotal PEDFIC 1 study, 90% of placebo and 76.2% of Bylvay patients were already receiving Ursodiol.
- Other PFIC options include surgical options such as nasobiliary drainage, partial external biliary diversion, and liver transplant.
- The PEDFIC 1 study only enrolled patients with PFIC type 1 or 2. PEDFIC 2 is an ongoing open-label extension of PEDFIC 1 and includes patients with other types of PFIC; however, results are not yet available.

- Bylvay will not work on PFIC type 2 with ABCB11 variants that encode for absence of BSEP-3 since Bylvay acts on the bile acid transporter. Therefore, in patients missing the BSEP-3 transporter, Bylvay may not inhibit the bile salt export pump.

*Appendix E: Observer-Reported Outcome (ObsRO) Instrument for Pruritus*

- Used to measure patients' scratching as observed by their caregiver twice daily (once in the morning and once in the evening)
- Scratching was assessed on a 5 point scale (0-4):
  - 0: no scratching
  - 1: a little scratching
  - 2: medium scratching
  - 3: a lot of scratching
  - 4: worst possible scratching

*Appendix F: Genetic Confirmation of PFIC*

- PFIC 1
  - Protein deficiency: FIC1
  - Mutated gene: ATP8B1
- PFIC 2
  - Protein deficiency: BSEP
  - Mutated gene: ABCB11

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose																		
PFIC	<p>The recommended dose is 40 mcg/kg PO AM with a meal. If there is no improvement in pruritus after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg PO QD not to exceed a total daily dose of 6 mg.</p> <p>Bylvay oral pellets are intended for use by patients weighing &lt; 19.5 kg, while the capsules are intended for use by patients weighing ≥ 19.5 kg.</p> <p><b>Recommended dosage/quantity for 40 mcg/kg/day:</b></p> <table border="1"> <thead> <tr> <th>Body weight (kg)</th> <th>Total daily dose (mcg)</th> </tr> </thead> <tbody> <tr> <td>≤ 7.4</td> <td>200 (1 oral pellet)</td> </tr> <tr> <td>7.5 to 12.4</td> <td>400 (2 oral pellets)</td> </tr> <tr> <td>12.5 to 17.4</td> <td>600 (3 oral pellets)</td> </tr> <tr> <td>17.5 to 25.4</td> <td>800 (2 capsules)</td> </tr> <tr> <td>25.5 to 35.4</td> <td>1,200 (1 capsule)</td> </tr> <tr> <td>35.5 to 45.4</td> <td>1,600 (2 capsules)</td> </tr> <tr> <td>45.5 to 55.4</td> <td>2,000 (3 capsules)</td> </tr> <tr> <td>≥ 55.5</td> <td>2,400 (2 capsules)</td> </tr> </tbody> </table>	Body weight (kg)	Total daily dose (mcg)	≤ 7.4	200 (1 oral pellet)	7.5 to 12.4	400 (2 oral pellets)	12.5 to 17.4	600 (3 oral pellets)	17.5 to 25.4	800 (2 capsules)	25.5 to 35.4	1,200 (1 capsule)	35.5 to 45.4	1,600 (2 capsules)	45.5 to 55.4	2,000 (3 capsules)	≥ 55.5	2,400 (2 capsules)	6 mg/day
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≥ 55.5	2,400 (2 capsules)																			

**VI. Product Availability**

- Oral pellets: 200 mcg, 600 mcg
- Capsules: 400 mcg, 1,200 mcg

**VII. References**

1. Bylvay Prescribing Information. Boston, MA: Albireo Pharma, Inc.; July 2021. Available at: <https://www.bylvay.com/pdf/Bylvay-PI-w-IFU-final-dated-July-2021.pdf>. Accessed August 5, 2021.
2. This study will investigate the efficacy and safety of A4250 in children with PFIC 1 or 2 (PEDFIC 1). ClinicalTrials.gov. Available at: <https://clinicaltrials.gov/ct2/show/NCT03566238>. Accessed August 5, 2021.
3. Long term safety & efficacy study evaluating the effect of A4250 in children with PFIC (PEDFIC 2). ClinicalTrials.gov. Available at: <https://clinicaltrials.gov/ct2/show/NCT03659916>. Accessed February 9, 2021. Albireo.
4. Albireo phase 3 trial meets both primary endpoints for odevixibat in PFIC. Press release available at: <https://ir.albireopharma.com/news-releases/news-release-details/albireo-phase-3-trial-meets-both-primary-endpoints-odevixibat>. Executive summary available at: <https://ir.albireopharma.com/static-files/d3df0f8f-336f-45eb-b6df-2d08e5e99596>. Published September 8, 2020. Accessed February 9, 2021.
5. Davit-Spraul A, Gonzales E, Baussan C, and Jacquemin E. Progressive familial intrahepatic cholestasis. Orphanet Journal of Rare Diseases. 2009; 4:1. doi:10.1186/1750-1172-4-1.
6. Gunaydin M and Cil A. Progressive familial intrahepatic cholestasis: Diagnosis, management, and treatment. Hepatic Medicine: Evidence and Research. 2018; 10: 95-104.
7. Baker A, Kerkar N, Todorova L, Kamath BM, and Houwen RHJ. Systematic review of progressive familial intrahepatic cholestasis. Clinics and Research in Hepatology and Gastroenterology. 2019; 43: 20-36.
8. Hirschfield GM, Heathcote EJ, and Gerswhin ME. Pathogenesis of cholestatic liver disease and therapeutic approaches. Reviews in Basic and Clinical Gastroenterology and Hepatology. 2010; 139(5): 1481-1496.
9. Progressive Familial Intrahepatic Cholestasis Advocacy and Resource Network. Diagnosis and treatment. Available at <https://www.pfic.org/diagnosis-and-treatment-of-pfic/>. Accessed August 8, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	04.13.21	05.21
Drug is now FDA approved - criteria updated per FDA labeling: modified age restriction; removed minimum body weight restriction; updated dosing requirements to include allowable escalations; references reviewed and updated.	07.21.21	08.21
RT1: added requirement for documentation of current body weight; added appendices D-F; references reviewed and updated.	08.31.21	11.21

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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