Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 05/01/2023**
Policy Number: PA.CP.PHAR.528	**Effective Date: 10/2021** **Revision Date: 04/2023**
Policy Name: Odevixibat (Bylvay)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

2Q 2023 annual review: no significant changes; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Odevixibat (Bylvay)

Reference Number: PA.CP.PHAR.528
Effective Date: 10/2021
Last Review Date: 04/2023

Revision Log

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 PA Health & Wellness® 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, 2, or 3 (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., ≥ 2 on 0 to 4 scale);
   b. Serum bile acids ≥ 100 µmol/L;
2. Prescribed by or in consultation with a hepatologist or gastroenterologist;
3. Age ≥ 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, rifampin, 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 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   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): PA.CP.PMN.53

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 – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ABCB11: ATP binding cassette subfamily B member 11
BSEP-3: bile salt export pump 3
FDA: Food and Drug Administration
IBAT: ileal bile acid transporter
ObsRO: observer-reported outcome
PFIC: progressive familial intrahepatic

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®)*	15-30 mg/kg/day	30 mg/kg/day
Example of therapies for pruritus: anthistamine, rifampin, cholestyramine	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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, rifampin, 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	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. Bylvay oral pellets are intended for use by patients weighing < 19.5 kg, while the capsules are intended for use by patients weighing ≥ 19.5 kg. **Recommended dosage/quantity for 40 mcg/kg/day**:	6 mg/day

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)

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.; October 2022. Available at: https://bylvay.com/. Accessed February 4, 2023.
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.
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 February 4, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/2021	
2Q 2022 annual review: modified rifampicin references to rifampin as there are no rifampicin products currently marketed; references reviewed and updated.	04/2022	
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023	