Clinical Policy: Odevixibat (Bylvay)

Reference Number: ERX.SPA.431
Effective Date: 07.20.21
Last Review Date: 08.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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., ≥ 2 on 0-4 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, rifampicin, cholestyramine), unless clinically significant adverse effects are experienced or all are contraindicated;
7. 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Progressive Familial Intrahepatic Cholestasis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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. 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
BSEP: bile salt export pump protein
FDA: Food and Drug Administration
PFIC: progressive familial intrahepatic cholestasis

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, rifampicin, 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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PFIC	The recommended dose is 40 mcg/kg PO QD. 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.; July 2021. Available at: https://www.bylvay.com/pdf/Bylvay-PI-w-IFU-final-dated-July-2021.pdf. Accessed July 21, 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 February 9, 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. 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.

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

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.