BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

BYLVAY™ (odevixibat) oral

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Bylvay (odevixibat) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hepatologist or Gastroenterologist.

  2. Individual is 3 months of age or older.

  3. Individual has a confirmed diagnosis of pruritis from progressive familial intrahepatic cholestasis (PFIC).

  4. There is genetic confirmation of PFIC type 1 or type 2

5. Individual does **not** have **ANY** of the following:
    a. *ABC11* gene variant that results in a non-functioning or complete absence of bile salt export pump protein (BSEP-3)
    b. Surgical history of disruption of enterohepatic circulation (biliary diversion surgery) within the previous 6-months
    c. Liver transplantation or liver transplantation is planned for within the next 6-months
    d. Past medical history or ongoing chronic diarrhea
    e. Uncontrolled, recalcitrant pruritic condition other than from PFIC
    f. Decompensated liver disease
    g. Past medical history or ongoing presence of other types of liver disease

6. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
    a. Fat-soluble vitamins (A, D, E, and K) levels
    b. Serum bile acids.

7. **For individuals 3 years of age or older** documented failure, contraindication or intolerance to Cholestyramine

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Bylvay (odevixibat) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Hepatologist or Gastroenterologist

2. Individual's condition has responded while on therapy
    a. Response is defined as **ALL** of the following:
        i. Achieved and maintains a reduction over baseline in itching or scratching rated by the individual or caregiver as none or little
        ii. No evidence of itching or scratching rated by the individual or caregiver as medium, "a lot," or worst
        iii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. Individual has not developed any significant adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Persistent or recurrent liver test abnormalities in alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, and International Normalized Ratio
        ii. Hepatic decompensation event such as variceal hemorrhage, ascites, hepatic encephalopathy
        iii. Persistent diarrhea
        iv. Persistent or worsening fat-soluble vitamin deficiency despite supplementation

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Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Bylvay (odevixibat) is a reversible inhibitor of the ileal bile acid transporter (IBAT) and is indicated for the treatment of pruritus in patients 3-months of age and older with progressive familial intrahepatic cholestasis (PFIC). Bylvay (odevixibat) 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).

Odevixibat decreases the reabsorption of bile acids (primarily the salt forms) from the terminal ileum. Pruritus is a common symptom in patients with PFIC and the pathophysiology of pruritus in patients with PFIC is not completely understood. Although the complete mechanism by which odevixibat improves pruritus in PFIC 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.

Progressive familial intrahepatic cholestasis (PFIC) is a heterogeneous group of disorders, characterized by defective secretion of bile acids or other components of bile. It presents in infancy or childhood and is associated with growth failure and progressive liver disease. There are four type of PFIC.

PFIC type 1, is also known as Byler disease and Greenland familial cholestasis, is caused by a mutation in the P-type ATPase gene (*ATP8B1*), *FIC1.* PFIC type 2 is similar to Byler disease clinically but occurs in non-Byler families, mainly in the Middle East and Europe. It is caused by defects in the *ABCD11* gene that codes for the sister P-glycoprotein (SPGP), also known as bile salt export pump (BSEP). Intractable pruritus is a dominant feature of PFIC types 1 and 2 and both are associated with life-threatening cholestasis. PFIC type 3, involves mutations in the ABCB4 gene (also known as multidrug resistance protein-3 P-glycoprotein [MDR3 or PGY3]). PFIC type 4 involves mutations in the *TJP2* gene that expresses tight junction protein 2 and resultant failure of claudin1 (CLDN1) localization.

Overall management of patients with PFIC includes addressing nutritional needs, managing pruritus caused by chronic cholestasis, and supplementation of fat-soluble vitamins. In all forms of PFIC use of ursodeoxycholic acid, may improve liver function in some patients, especially those with PFIC 3 disease and may relieve the pruritus associated with the disorder. Severe pruritus associated with PFIC 1 and 2 is frequently unresponsive to treatment with ursodeoxycholic acid or antihistamines. Novel ileal bile acid transport (IBAT) inhibitors may be effective in reducing the severity of pruritus in patients with cholestasis by interrupting enterohepatic circulation of bile acids. Surgical diversion procedures to interrupt enterohepatic circulation of bile acids may be successful in alleviating severe pruritus. Liver transplantation is generally curative for patients with PFIC 1, 2, and 4. It is an important option for patients with end-stage liver disease due to PFIC, and for some patients with pruritus that is unresponsive.

Resources:

Bylvay (odevixibat) product information, revised by Albireo Pharma, Inc. 07-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 19, 2022.

Roy-Chowdhury J, Roy-Chowdhury N. Inherited disorders associated with conjugated hyperbilirubinemia. In: UpToDate, Lindor KD, Grover S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on December 06,2021. Accessed July 19, 2022.

Poupon R, Chopra S. Pruritus associated with cholestasis. In: UpToDate, Lindor KD, Grover S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on February 16, 2021. Accessed July 19, 2022.