BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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BYLVAY™ (odevixibat) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

BYLVAY™ (odevixibat) oral

Criteria:

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

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

  2. Individual is 3 months of age or older

  3. 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. Elevated serum bile acids

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

  8. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Bylvay (odevixibat) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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

  2. Individual's condition has responded
     a. Response is defined as **ALL** of the following:

i. Achieved and maintains a reduction in itching or scratching rated by the individual or caregiver as none or little over baseline
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

5. There are no significant interacting drugs

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 a Non-cancer Medications**

  2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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.

BYLVAY™ (odevixibat) oral

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 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 on August 07, 2021.

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. Accessed on August 07, 2021.

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. Accessed on August 07, 2021.

Lindor KD, Bowlus CL, Boyer J, et al.: Primary Biliary Cholangitis: 2018 Practice Guidance from The American Association of the Study of Liver Diseases. Hepatol 2019; 69 (1): 394-419. Accessed August 08, 2021.

ClinicalTrials,gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT03566238. A double-blind, randomized, placebo-controlled, phase 3 study to demonstrate efficacy and safety of A4250 in children with progressive familial intrahepatic cholestasis types 1 and 2 (PEDF IC 1). Last updated September 17, 2020. Available from: http://clinicaltrials.gov. Accessed August 07, 2021.