Bylvay (odevixibat)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Bylvay (odevixibat) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

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

Limitation of Use

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).

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- Initial requests: Genetic testing results confirming a diagnosis of progressive familial intrahepatic cholestasis (PFIC) type 1, 2, or 3.
- Continuation requests: Chart notes or medical records documenting a benefit from therapy (e.g., improvement in pruritis).

Exclusions

Coverage will not be provided for members who have PFIC type 2 with variants in the *ABCB11* gene that predict non-functional or complete absence of the bile salt export pump protein (BSEP-3).

Prescriber Specialties
The medication must be prescribed by or in consultation with a hepatologist.

Criteria for Initial Approval
Pruritus in progressive familial intrahepatic cholestasis (PFIC)
Authorization of 6 months may be granted for treatment of pruritis in progressive familial intrahepatic cholestasis (PFIC) when all of the following criteria are met:
A. Member has confirmed molecular diagnosis of PFIC type 1, 2, or 3
B. Member does not have any other concomitant liver disease (e.g., biliary atresia, benign recurrent intrahepatic cholestasis [BRIC], liver cancer, alternate non-PFIC related etiology of cholestasis)
C. Member has not received a liver transplant.
D. Member is 3 months of age or older.

Continuation of Therapy
Authorization of 12 months may be granted for all members (including new members) requesting continuation of therapy when the member is experiencing benefit from therapy (e.g., improvement in pruritis).

Bylvay is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits:

Medication	Standard Limit	FDA-recommended dosing
Bylvay (odevixibat) pellets 200 mcg	60 per 30 days	40 mcg/kg once daily 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 once daily not to exceed a total daily dose of 6 mg.
Bylvay (odevixibat) pellets 600 mcg	120 per 30 days	
Bylvay (odevixibat) capsule 400 mcg	60 per 30 days	
Bylvay (odevixibat) capsule 1200 mcg	150 per 30 days	

CLINICAL RATIONALE

Background
Progressive familial intrahepatic cholestasis (PFIC) is a group of rare autosomal recessive genetic disorders that results in the inability to appropriately form and excrete bile from hepatocytes that can lead to cirrhosis and end-stage liver disease. PFIC usually develops in infancy, although it can develop into young adulthood. Most patients with PFIC require biliary diversion surgery or liver transplant by 30 years of age. There are three classic types of PFIC. PFIC 1 is caused by mutations of the ATP8B1 gene, encoding the familial intrahepatic cholestasis 1 protein. PFIC 2 is the result of mutations in the ABCB11 gene, reducing the apical membrane expression of bile salt export pump. PFIC 3 is caused by variations in the gene that encodes the multidrug resistance class 3 glycoprotein. Type 1, type 2, and type 3 are the most common; however, due to advances in deoxyribonucleic acid (DNA) sequencing, new forms of this disease (i.e., PFIC 4, PFIC 5, PFIC associated with MYO5B defects) have been identified. PFIC is typically diagnosed using

liver function tests (e.g., gamma-glutamyltransferase [GGT], aspartate aminotransferase [AST], alanine transaminase [ALT]), bile acid tests, liver biopsy, and genetic testing. The age of onset and severity is variable, ranging from neonatal period in PFIC 2 to adulthood/late adolescence in PFIC 3. The main clinical features of PFIC include cholestasis, jaundice, and pruritis. Cholestatic liver disease can also lead to symptoms such as a swollen abdomen, dark yellow or brown urine, acholic stools (i.e., stools that are pale, grey, or white in color), bleeding or easy bruising, poor growth, and vitamin deficiencies.

Pharmacologic treatment options for patients with PFIC are off label and include Ursodiol (ursodeoxycholic acid), bile acid sequestrants, and agents for the symptomatic relief of pruritus, such as antihistamines and Rifampin (rifampicin). Not all patients respond to these approaches, however, and generally only partial relief from itching is achieved. Invasive surgery, such as ileal bypass, partial external biliary diversion, or partial internal biliary diversion may be needed to lower circulating bile acid concentrations. Liver failure and intractable pruritus are common, and liver transplantation may be needed, most often in patients with PFIC 2. In July 2021, Bylvay (odevixibat) was FDA approved as the first medication for the treatment of pruritus in patients with PFIC and is indicated for patients 3 months of age and older. Bylvay (odevixibat) works by reversibly inhibiting the ileal bile acid transporter (IBAT) which decreases reabsorption of bile acids from the terminal ileum of the intestine. Bylvay is available as 200 mcg oral pellets, 600 mcg oral pellets, 400 mcg oral capsules, and 1,200 mcg oral capsules. Bylvay pellets are intended for use by patients weighing < 19.5 kg, and Bylvay capsules are intended for use by patients weighing ≥ 19.5 kg. The recommended dosage of Bylvay is 40 mcg/kg orally once daily in the morning with a meal. If there is no improvement in pruritis after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once daily not to exceed a total daily dose of 6 mg.

Efficacy

The efficacy of Bylvay was evaluated in two clinical trials, PEDFIC 1 and PEDFIC 2. PEDFIC 1 was a 24-week, Phase 3, randomized, double-blind, placebo-controlled trial that evaluated pruritis and bile acid reduction in patients with PFIC types 1 and 2. The trial enrolled 62 patients 6 months of age to 17 years with genetically confirmed PFIC 1 or 2 with a history of significant pruritis in the 2 weeks prior to enrollment. Exclusion criteria included pathologic variations of the *ABCB11* gene that predict complete absence of the BSEP protein, INR > 1.4, ALT or total bilirubin >10 times the upper limit of normal, liver transplant, biliary diversion surgery within 6 months of the start of the screening period, and prior hepatic decompensation events or other concomitant liver disease. The primary endpoint was change in pruritus and bile acid reduction (defined as bile acid reduction ≥70% or reaching a bile acid level ≤70 µmol/L). Bylvay met both its pruritus (p=0.004) and serum bile acid (p=0.003) primary endpoints. PEDFIC 2 is an ongoing, long-term (72 weeks), open-label Phase 3 extension study in patients with PFIC types 1, 2, or 3. This trial included 56 patients from PEDFIC 1 and 23 additional patients, totally 79 patients. Preliminary results at Week 48 showed continued reductions in serum bile acid levels, improvements in pruritus assessments, growth, and other markers of liver function in patients.

Safety

In PEDFIC 1, the incidence of treatment-related adverse events was 33.3% with Bylvay and 15% with placebo. The most common reactions were diarrhea, increased ALT/AST, vomiting, abdominal pain, and fat-soluble vitamin (FSV) deficiency. Treatment-related adverse events of diarrhea or frequent bowel movement occurred in 9.5% of Bylvay-treated patients and 5% of placebo-treated patients; one patient in the Bylvay 120 mcg/kg/day arm discontinued due to an adverse event (i.e., diarrhea). No deaths or drug-related serious adverse events were reported. In PEFIC 2, treatment-emergent adverse events (TEAEs) occurred in 79% of patients and most were mild to moderate in severity and assessed as unrelated to Bylvay. Four patients discontinued Bylvay due to TEAEs, and of these one was reported to be related to Bylvay treatment (i.e., diarrhea). Bylvay carries warnings for liver test abnormalities, diarrhea, and FSV deficiency.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- Not applicable (N/A)

REFERENCES

- Bylvay [package insert]. Boston, MA: Albireo Pharma, Inc.; July 2021
- Amirneni S, Haep N, Gad MA, Soto-Gutierrez A, Squires JE, Florentino RM. Molecular overview of progressive familial intrahepatic cholestasis. World J Gastroenterol. 2020; 26(47):7470-7484. doi: 10.3748/wjg.v26.i47.7470
- Baker A, Kerkar N, Todorova L, Kamath BM, Houwen RH. Systematic review of progressive familial intrahepatic cholestasis. Clin Res Hepatol Gastroenterol. 2019;43(1):20-36. doi: 10.1016/j.clinre.2018.07.010
- Bylvay. Prescribing information. Albireo Pharma, Inc.; July 2021. Accessed August 4, 2021.
- Food and Drug Administration (FDA). Developing products for rare diseases & conditions. December 20, 2018. Accessed August 4, 2021. https://www.fda.gov/industry/developing-products-rare-diseases-conditions
- Food and Drug Administration (FDA). Drugs@FDA. Accessed August 5, 2021. http://www.accessdata.fda.gov/scripts/cder/drugsatfda
- Food and Drug Administration (FDA). Rare pediatric disease priority review voucher program. November 2, 2017. Accessed July 9, 2021. https://www.fda.gov/industry/developing-products-rare-diseases-conditions/rare-pediatric-disease-rpd-designation-and-voucher-programs
- Institute for Clinical and Economic Review (ICER). Accessed August 5, 2021. https://icer.org/
- National institute of Health and Care Excellence (NICE). Accessed August 5, 2021a. http://www.nice.org.uk
- National institute of Health and Care Excellence (NICE). Odevixibat for progressive familial intrahepatic cholestasis [ID1570]. Accessed August 5, 2021b. https://www.nice.org.uk/guidance/indevelopment/gid-hst10043
- PFIC Advocacy & Resource Network. Accessed August 6, 2021. https://www.pfic.org/
- RxPipeline. Accessed August 16, 2021. https://www.caremark.com/wps/portal/client
- Srivastava A. Progressive familial intrahepatic cholestasis. J Clin Exp Hepatol. 2014;4(1):25-36. doi: 10.1016/j.jceh.2013.10.005
- Thompson RJ, Baumann U, Czubkowski P, et al. Efficacy and safety of odevixibat, an ileal bile acid transporter inhibitor, in children with progressive familial intrahepatic cholestasis types 1 and 2: results from PEDFIC 1, a randomized, double-blind, placebo-controlled phase 3 trial. Abstract presented at: American Association of Liver Diseases; November 15, 2020; Accessed August 16, 2021. https://assets.website-files.com/5f3d77cd56d46907a50fb8d9/5f9d9c2057efc43f55b78db7_2020%20TLMdX%20Late-breaking%20Abstracts-%20Oct%2030.pdf
- Thompson R, Artan R, Baumann U, et al. Odevixibat effects on cholestasis-related parameters: analysis of pooled data from the PEDFIC 1 and PEDFIC 2 studies in children with progressive familial intrahepatic cholestasis. Poster presented at the International Liver Congress; June 23-26, 2021; virtual.

*Some content reprinted from CVSHealth

POLICY HISTORY

Policy #: 05.04.42
Original Effective Date: November 12, 2021
Reviewed: October 2022
Revised:
Current Effective Date: November 12, 2021