PRIOR AUTHORIZATION (PA) CONSIDERATIONS CHECKLIST

Prescribers and office staff can use this checklist of considerations when submitting a prior authorization to a health plan for patients prescribed Bylvay

This checklist is for informational purposes only and lists coverage criteria that may be required or helpful for PA submissions. Provision of this information does not constitute medical or legal advice and the information may be incomplete or inapplicable for some health plans. Including the below information in a PA submission does not guarantee approval by a health plan and is not intended to be a substitute for or an influence on the independent clinical decision of the prescribing healthcare professional. Ipsen cannot guarantee that these are the criteria used by health plans or pharmacy benefit managers when making PA decisions. It is recommended that the prescribing healthcare professional or staff check the plan's specific coverage criteria and PA requirements, as these can vary by health plan and with time.

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IPSEN CARES serves as a central point of contact dedicated to assisting patients, providers, and staff.
Call (866) 435-5677, Monday-Friday, 8 AM - 8 PM ET, fax (855) 465-3820, or visit our website IPSENCARES.com.

IPSEN CARES can help provide information on how to submit a PA to the patient's specific health plan. Please consider enrolling your patient into IPSEN CARES should you require PA support.

Please note that IPSEN CARES will not submit a PA on behalf of the prescriber or office. IPSEN CARES can help provide information and templates to support the submission of a PA to the patient's health plan.

INDICATION

BYLVAY is an ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of:

- cholestatic pruritus in patients ≥12 months of age with Alagille syndrome (ALGS)
- pruritus in patients ≥3 months of age with progressive familial intrahepatic cholestasis (PFIC)

Limitation of Use:

BYLVAY may not be effective in a subgroup of PFIC type 2 patients with specific *ABCB11* variants resulting in non-functional or complete absence of the bile salt export pump protein.

IMPORTANT SAFETY INFORMATION

Contraindications

IBAT inhibitors, including BYLVAY, are contraindicated in patients with prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

Please see Important Safety Information throughout and full Prescribing Information.

Example of Common Coverage Policy Criteria for Bylvay

When preparing the PA, confirm the health plan's specific coverage policy criteria requirements and document how long the initial PA remains valid, as this can vary across plans from ~3 months to 1 year.[1-4]

Clinical Presentation and Diagnosis

Patients can be clinically diagnosed with PFIC without a known pathogenic variant.[5] Clinical presentation of PFIC can include jaundice, pruritus, elevated serum bile acid (SBA) values, malabsorption, and failure to thrive.[6] Genetic screening may not identify unknown pathogenic variants associated with PFIC.[7]

Age:

- ❑ Patient is aged ≥3 months[1-3]

Evidence of pruritus:

- ❑ Prescriber-confirmed moderate-to-severe pruritus[1-4]

Health plans may require that the following criteria be met for initial PA approval.

Medical Criteria

Clinical Manifestations

- ❑ Cholestasis, jaundice, and pruritus[2]

Laboratory results

- ❑ SBA concentration above the upper limit of the normal reference range for the reporting laboratory[2,4]
- ❑ Liver function tests (LFTs): alanine aminotransferase and aspartate aminotransferase[1,3,10]
- ❑ Serum fat-soluble vitamin (FSV) levels[1,3]
  - – Prescriber agrees to monitor LFTs and serum FSV levels during treatment

Treatment history

- ❑ Documentation of inadequate response to or failure of other conventional treatments for symptomatic relief of pruritus[1-4]
- ❑ Tried at least 2 systemic medications (cholestyramine, colesevelam, or colestipol; naltrexone; rifampicin; sertraline, ursodeoxycholic acid; antihistamine) unless contraindicated[1-4]
- ❑ Documentation of any reasons why other conventional treatments cannot be used[1-4]
- ❑ Bylvay medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in PFIC[2,4]

Genetic testing

- ❑ Some plans may require genetic testing. Please include any genetic testing that has been completed.[2-4]
- ❑ Genetic variations in *ATP8B1*, *ABCB11*, *ABCB4*, *TJP2*, *NR1H4*, *MYO5B, SLC51A, USP53, KIF12, ZFYVE19, SEMA7A, VPS33B, PSKH1*[2,8]
- ❑ Limitations of Use: PFIC type 2 cases with biallelic *ABCB11* variants (*E297G*, *D482G*, *G238V*, *G982R*, *R1153C*, and *R1268Q*), which result in a nonfunctional or completely absent bile salt export pump (BSEP) protein[1,4,9-11]

Confirmation of no liver disease

- ❑ No cirrhosis[1,2]
- ❑ No portal hypertension[1,2]
- ❑ No prior or active hepatic decompensation event (eg, variceal hemorrhage, ascites, and hepatic encephalopathy)[1,2]
- ❑ No history of liver transplant[12]

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions

Hepatotoxicity

BYLVAY treatment is associated with a potential for drug-induced liver injury (DILI). In the PFIC and ALGS trials, treatment-emergent elevations or worsening of liver tests occurred. Of the six patients who experienced DILI, two underwent liver transplant. Obtain baseline liver tests because some ALGS and PFIC patients have abnormal liver tests at baseline and monitor patients frequently for the first 6 to 8 months, and as clinically needed thereafter, for elevations in liver tests, for the development of liver-related adverse reactions, and for physical signs of hepatic decompensation. If liver test abnormalities or signs of clinical hepatitis occur in the absence of other causes, consider dose reduction or treatment interruption. Permanently discontinue BYLVAY if a patient experiences the following: persistent or recurrent liver test abnormalities, or upon rechallenge, signs and symptoms consistent with clinical hepatitis, or a hepatic decompensation event.

Please see Important Safety Information throughout and full Prescribing Information.

Example of Common Coverage Policy Criteria for Bylvay

When requesting reauthorization, review the health plan's specific coverage policy criteria requirements for changes, and, once re-approved, document how long the reauthorization remains valid.[1-4]

Additional Information That May Be Required for Continuation of Therapy

When requesting reauthorization, confirm the health plan's specific criteria and document how long the subsequent authorization remains valid as this can vary across plans.[1-4]

- ❑ Documented response to therapy (for example, improved pruritus and decreased SBA) as determined by the prescriber. 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 daily dosage of 6 mg/day.[1-4,10]
- ❑ No cirrhosis, portal hypertension, history of hepatic decompensation event, or liver transplant[1,2,12]
- ❑ Bylvay medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in PFIC[2,4]
- ❑ Prescriber agrees to monitor LFTs and serum FSV levels during treatment[1,3]

Always be mindful of following each health plan's specific criteria and processes for submitting PAs for patients prescribed Bylvay. Consider including the following literature as supporting documentation for Bylvay PA submissions:

- Bylvay (odevixibat) Prescribing Information. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; 2025. Available at: https://d2rkmuse97gwnh.cloudfront.net/a88aa6d6-3ca0-4362-a711-d53c45ae33ff/5f7d23c0-f85b-4f9a-907a-3f2fa18aa260/5f7d23c0-f85b-4f9a-907a-3f2fa18aa260_source__v.pdf
- Thompson RJ, Arnell H, Artan R, et al. Odevixibat treatment in progressive familial intrahepatic cholestasis: a randomised, placebo-controlled, phase 3 trial. *Lancet Gastroenterol Hepatol*. 2022;7(9):830-842. Available at: https://www.thelancet.com/journals/langas/article/PIIS2468-1253(22)00093-0/fulltext
- Thompson RJ, Artan A, Baumann U, et al. Interim results from an ongoing, open-label, single-arm trial of odevixibat in progressive familial intrahepatic cholestasis. *JHEP Rep*. 2023;5(8):100782. Available at: https://www.jhep-reports.eu/article/S2589-5559(23)00113-1/fulltext

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

Hepatotoxicity (continued)

The safety and effectiveness of BYLVAY have not been established in patients with decompensated cirrhosis. Monitor patients with compensated cirrhosis or portal hypertension more frequently and discontinue if hepatic decompensation occurs. IBAT inhibitors, including BYLVAY, are contraindicated in patients with prior or active hepatic decompensation events.

Please see Important Safety Information throughout and full Prescribing Information.

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Example of Common Coverage Policy Criteria for Bylvay

When preparing the PA, confirm the health plan's specific coverage policy criteria requirements and document how long the initial PA remains valid, as this can vary across plans from ~3 months to 1 year.[1-4]

Clinical Presentation and Diagnosis

Patients can be clinically diagnosed with ALGS even in the absence of a known pathogenic variant.[13] Clinical features may include cholestasis, pruritus, elevated serum bile acid (SBA) values, cardiac defect, skeletal abnormality, ophthalmic abnormality, or characteristic facial features.[14] Genetic screening may not identify all pathogenic variants associated with ALGS.[13]

Age:
- ❑ Patient is aged ≥12 months[1,2]

Clinical diagnosis:
- ❑ Bile duct paucity and at least 3 major clinical features of ALGS[1]

Evidence of pruritus:
- ❑ Prescriber-confirmed pruritus (some PAs require documents moderate-to-severe pruritus)[1-4]

Health plans may require that the following criteria be met for initial PA approval.

Medical Criteria

Clinical Manifestations
- ❑ Cholestasis, cardiac defect, skeletal abnormality, ophthalmic abnormality, or characteristic facial features[1]

Laboratory results
- ❑ SBA concentration above the upper limit of the normal reference range for the reporting laboratory[2,4]
- ❑ Liver function tests (LFT): alanine aminotransferase and aspartate aminotransferase[1,3,10]
- ❑ Serum fat-soluble vitamin (FSV) levels[1,3]
  - Prescriber agrees to monitor LFTs and serum FSV levels during treatment

Treatment history
- ❑ Documentation of inadequate response to or failure of other conventional treatments for symptomatic relief of pruritus[1-4]
- ❑ Tried at least 2 systemic medications (fenofibrate, cholestyramine, colesevelam, or colestipol; naltrexone; rifampicin; sertraline; ursodeoxycholic acid; antihistamine) unless contraindicated[1-4]
- ❑ Documentation of any reasons why other conventional treatments cannot be used[1-4]
- ❑ Bylvay medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in ALGS[2,4]

Genetic Testing
- ❑ Some plans may require genetic testing. Please include any genetic testing that has been completed.[2-4]
- ❑ Genetic loss-of-function variant in *JAG1* or *NOTCH2*[1,2,4]

Confirmation of no liver disease
- ❑ No cirrhosis[1,2]
- ❑ No portal hypertension[1,2]
- ❑ No prior or active hepatic decompensation event (eg, variceal hemorrhage, ascites, and hepatic encephalopathy)[1,2]
- ❑ No history of liver transplant[15]

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

Diarrhea

In the PFIC and ALGS clinical trials, diarrhea was reported more frequently in BYLVAY-treated patients compared to placebo. In the PFIC clinical trials, treatment interruption due to diarrhea occurred in 2 patients with 3 events. Treatment interruption due to diarrhea ranged between 3 to 7 days. One patient withdrew from the trial. In the ALGS clinical trial, no patients interrupted or discontinued treatment due to diarrhea.

If diarrhea occurs, monitor for dehydration and treat promptly. Interrupt dosing if a patient experiences persistent diarrhea. Restart BYLVAY at 40 mcg/kg/day when diarrhea resolves and increase the dose as tolerated if appropriate. If diarrhea persists and no alternate etiology is identified, stop treatment.

Example of Common Coverage Policy Criteria for Bylvay

When requesting reauthorization, review the health plan's specific coverage policy criteria requirements for changes, and, once re-approved, document how long the reauthorization remains valid.[1-4]

Additional Information That May Be Required for Continuation of Therapy

When requesting reauthorization, confirm the health plan's specific criteria and document how long the subsequent authorization remains valid, as this can vary across plans.[1-4]

- ❑ Documented response to therapy (for example, improved pruritus and decreased SBA) as determined by the prescriber[1-4]
- ❑ No cirrhosis, portal hypertension, history of hepatic decompensation event, or liver transplant[1,2,15]
- ❑ Bylvay medication is prescribed by or in consultation with a hepatologist, gastroenterologist, or a physician who specializes in ALGS[2,4]
- ❑ Prescriber agrees to monitor LFTs and serum FSV levels during treatment[1,3]

Always be mindful of following each health plan's specific criteria and processes for submitting PAs for patients prescribed Bylvay. Consider including the following literature as supporting documentation for Bylvay PA submissions:

- Bylvay (odevixibat) Prescribing Information. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; 2025. Available at: https://d2rkmuse97gwnh.cloudfront.net/a88aa6d6-3ca0-4362-a711-d53c45ae33ff/5f7d23c0-f85b-4f9a-907a-3f2fa18aa260/5f7d23c0-f85b-4f9a-907a-3f2fa18aa260_source__v.pdf
- Ovchinsky N, Aumar M, Baker A, et al. Efficacy and safety of odevixibat in patients with Alagille syndrome (ASSERT): a phase 3, double-blind, randomised, placebo-controlled trial. *Lancet Gastroenterol Hepatol*. 2024;9(7):632-645. Available at: https://www.thelancet.com/journals/langas/article/PIIS2468-1253(24)00074-8/fulltext

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

Fat-Soluble Vitamin (FSV) Deficiency

Fat-soluble vitamins (FSV) include vitamin A, D, E, and K. PFIC and ALGS patients can have FSV deficiency at baseline. BYLVAY may affect absorption of FSVs. In clinical trials, new onset or worsening of existing FSV deficiency was reported more frequently in BYLVAY-treated patients compared to placebo.

Please see Important Safety Information throughout and full Prescribing Information.

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IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

Fat-Soluble Vitamin (FSV) Deficiency (continued)

Obtain baseline INR and FSV levels and monitor during treatment along with any clinical manifestations. If FSV deficiency is diagnosed, supplement with FSV. Discontinue BYLVAY if FSV deficiency persists or worsens despite adequate FSV supplementation and consider restarting once the patient is clinically stable.

If bleeding occurs, interrupt treatment with BYLVAY. Optimize treatment of FSV deficiency and consider restarting BYLVAY once the patient is clinically stable.

Adverse Reactions

The most common adverse reactions for BYLVAY in patients with PFIC are diarrhea, liver test abnormalities, vomiting, abdominal pain, and FSV deficiency.

The most common adverse reactions for BYLVAY patients with ALGS are diarrhea, abdominal pain, hematoma, and decreased weight.

Drug Interactions

For patients taking bile acid binding resins, take BYLVAY at least 4 hours before or 4 hours after taking a bile acid binding resin.

Use in Specific Populations

There are no human data on BYLVAY use in pregnant persons to establish a drug-associated risk of major birth defects, miscarriage, or adverse developmental outcomes. Based on findings from animal reproduction studies, BYLVAY may cause cardiac malformations when a fetus is exposed during pregnancy. There is a pregnancy exposure registry that monitors pregnancy outcomes in persons exposed to BYLVAY during pregnancy. For more information, please call 1-855-463-5127.

To report SUSPECTED ADVERSE REACTIONS, contact Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information.

References: 1. BlueCross BlueShield Federal Employee Program. Bylvay (odevixibat) Prior-approval requirements. Accessed October 22, 2025. https://info.caremark.com/content/dam/enterprise/caremark/microsites/dig/pdfs/pa-fep/fep-criteria/FEP_Criteria_Bylvay.pdf **2.** Cigna Healthcare. Hepatology – Bylvay Prior Authorization Policy. July 30, 2025. Accessed October 26, 2025. https://static.cigna.com/assets/chcp/pdf/coveragePolicies/cnf/cnf_690_coveragepositioncriteria_hepatology_bylvay_pa.pdf **3.** Highmark Wholecare. Prior authorization criteria. Bylvay (odevixibat). June 2025. Accessed October 22, 2025. https://fm.formularynavigator.com/FormularyNavigator/DocumentManager/Download?clientDocumentId=sg-K3ACSQUy7tJiRnp-8GA **4.** UnitedHealthcare Pharmacy. Clinical pharmacy programs. Prior authorization/medical necessity. Bylvay™ (odevixibat). November 1, 2024. Accessed October 22, 2025. https://www.uhcprovider.com/content/dam/provider/docs/public/prior-auth/drugs-pharmacy/commercial/a-g/PA-Med-Nec-Bylvay.pdf **5.** LIVMARLI® (maralixibat). Prescribing information. Mirum Pharmaceuticals, Inc.; 2025. **6.** Henkel SA, Squires JH, Ayers M, Ganoza A, McKiernan P, Squires JE. Expanding etiology of progressive familial intrahepatic cholestasis. *World J Hepatol*. 2019;11(5):450-463. **7.** McKiernan P, Bernabeu JQ, Girard M, Indolfi G, Lurz E, Trivedi P. Opinion paper on the diagnosis and treatment of progressive familial intrahepatic cholestasis. *JHEP Rep*. 2023;6(1):100949 **8.** OMIM. Phenotypic Series - PS211600. Accessed November 13, 2025. https://www.omim.org/phenotypicSeries/PS211600 **9.** Wang L, Soroka CJ, Boyer JL. The role of bile salt export pump mutations in progressive familial intrahepatic cholestasis type II. *J Clin Invest*. 2002;110(7):965-972. **10.** Bylvay (odevixibat)® Prescribing information. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; 2025 **11.** Van Wessel DBE, Thompson R, et al. Genotype correlates with the natural history of severe bile salt export pump deficiency. *J Hepatol*. 2020;73(1):84-93. **12.** Thompson RJ, Arnell H, Artan R, et al. Odevixibat treatment in progressive familial intrahepatic cholestasis: a randomised, placebo-controlled, phase 3 trial. *Lancet Gastroenterol Hepatol*. 2022;7(9):830-842. **13.** Ayoub MD, Kamath BM. Alagille syndrome: current understanding of pathogenesis, and challenges in diagnosis and management. *Clin Liver Dis*. 2022;26(3):355-370. **14.** Diaz-Frias J, Kondamudi NP. Alagile syndrome. Accessed October 22, 2025. https://www.ncbi.nlm.nih.gov/books/NBK507827/ **15.** Ovchinsky N, Aumar M, Baker A, et al. Efficacy and safety of odevixibat in patients with Alagille syndrome (ASSERT): a phase 3, double-blind, randomised, placebo-controlled trial. *Lancet Gastroenterol Hepatol*. 2024;9(7):632-645.

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