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**Review paper**

# Recommendations for the diagnosis and treatment of primary biliary cholangitis for 2026: Polish Expert Group on Primary Biliary Cholangitis

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## Abstract

The prevalence of primary biliary cholangitis (PBC) in Poland – 11.1 per 100,000 inhabitants – is approximately half the reported European prevalence. This low prevalence may reflect a lack of awareness regarding the disease, resulting in underdiagnosis. These recommendations are intended for both practicing physicians and health policy-making institutions, to standardize PBC diagnostic and therapeutic practices. The document outlines diagnostic criteria and treatment options, while also addressing management strategies for treatment failure. The recommendations are based on current international guidelines, expert knowledge, and experience. The Polish Expert Group on PBC was formed by members of the Polish Association for the Study of the Liver, the Polish Society of Epidemiologists and Infectious Disease Physicians, and the Central European Hepatologic Collaboration – bringing together specialists managing liver diseases. To reach a consensus, the Delphi method was employed. The final level of consensus among panel members for individual recommendations ranged from 96% to 100%.

**Key words:** liver, primary biliary cholangitis, seladelpar, elafibranor, ursodeoxycholic acid.

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## Introduction

Primary biliary cholangitis (PBC) is a rare, chronic, cholestatic liver disease characterized by the progressive, immune-mediated destruction of interlobular and septal bile ducts, which can lead to liver cirrhosis [1]. Although the first descriptions of the disease date back to the 19th century, it was first named "primary biliary cirrhosis" in 1949 [2]. In 2015, Beuers *et al.* [3] proposed changing the name to "primary biliary cholangitis" to better reflect the broader nature of the condition, which warrants the earliest possible diagnosis and treatment. This name was adopted in the guidelines of the European Association for the Study of the Liver (EASL) published in 2017 [4].

Over 90% of all PBC cases occur in women, typically after the age of 50, although the disease is increasingly being diagnosed in individuals under 40 [5].

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The pathogenesis of PBC remains unclear; however, the disease appears to be triggered by an interplay between genetic predisposition and environmental exposures [6]. A characteristic serological feature of PBC is the presence of M2-subtype antimitochondrial antibodies (AMA-M2) directed against the E2 subunit of the pyruvate dehydrogenase complex (PDC-E2) in biliary epithelial cells [7, 8]. In the AMA-negative form of the disease, the diagnosis can be confirmed based on the presence of specific antinuclear antibodies: anti-glycoprotein 210 (anti-gp210) and anti-speckled protein (anti-sp100); these are associated with a more aggressive disease course and a poorer prognosis [9]. Elevated alkaline phosphatase (ALP) activity is a key biochemical marker of cholestasis and – along with bilirubin levels – reflects the disease stage and progression rate [10]. PBC is typically asymptomatic in its early stages, with autoantibodies potentially serving as the only predictive indicator; clinical symptoms – most commonly pruritus and fatigue – develop at a later stage [11-13]. As the disease progresses, increasing fibrosis and structural remodeling of the liver lead to the development of cirrhosis [14].

Aggregated global estimates indicate a PBC prevalence of 14.6 per 100,000 inhabitants, with 22.3 per 100,000 in Europe [15, 16]. In contrast, the prevalence of diagnosed PBC in Poland – averaging 11.1 per 100,000 inhabitants – varies significantly, ranging from just 2.3 per 100,000 in the Wielkopolskie voivodeship to approximately 20 per 100,000 in the Podlaskie and Zachodniopomorskie voivodeships [17]. Such low prevalence rates and marked regional disparities likely stem from insufficient awareness and a lack of focus on diagnosing PBC. These recommendations aim to address this situation. They are addressed to both practicing physicians across various specialties and health policy-making institutions, to standardize PBC diagnostic and therapeutic protocols and align current medical knowledge with the realities of the Polish healthcare system.

The Polish Expert Group on Primary Biliary Cholangitis was formed by members of the Polish Association for the Study of the Liver, the Polish Society of Epidemiologists and Infectious Disease Physicians, and the Central European Hepatologic Collaboration – organizations bringing together doctors and scientists who specialize in liver diseases, including PBC, in Poland. To reach a consensus among the expert group members, the Delphi method involving three rounds of surveys was employed, resulting in agreement on the content of 17 key recommendation statements. The level of agreement (LoA) among panel members regarding each recommendation statement was determined as a percentage. All members of the expert group approved the final version of the recommendations.

## Screening (LoA: 97%)

Screening for PBC, involving the routine measurement of alkaline phosphatase activity, should cover all individuals over the age of 40, ideally within the framework of mass preventive programs such as "Moje Zdrowie" in Poland. If large-scale testing is not feasible, the screening program should at least include women aged 50 and over.

## Diagnosis (LoA: 98%)

Diagnostic evaluation for PBC may result in a diagnosis of definite or probable PBC, seronegative PBC, or a condition referred to as pre-PBC.

- A diagnosis of definite PBC is established when ALP activity exceeds the upper limit of normal (ULN) and anti-mitochondrial antibodies (AMA-M2) or PBC-specific antinuclear antibodies (ANA) – such as anti-gp210 and anti-sp100 – are present in the blood [4].
- A diagnosis of probable PBC is considered when normal ALP activity is accompanied by γ-glutamyl transferase (GGT) activity exceeding the ULN and the presence of AMA-M2, anti-gp210, or anti-sp100 antibodies in the blood. In such cases, demonstrating histological features typical of PBC in a liver biopsy is indicated to confirm the diagnosis [18].
- In cases of suspected seronegative PBC – where disease-specific autoantibodies are not detected despite elevated ALP activity – a detailed differential diagnosis is required given the high diagnostic uncertainty; establishing a diagnosis of PBC in these instances requires demonstrating histological features typical of PBC on liver biopsy.
- Pre-PBC is a condition characterized by the presence of AMA-M2 or PBC-specific ANA in the blood alongside normal ALP and GGT activity. While this does not allow for a diagnosis of the disease, it warrants monitoring of the activity of these enzymes at least once a year.

It should be emphasized that for all the aforementioned forms, differential diagnosis is required to rule out other causes of elevated ALP or GGT activity. The diagnostic significance of autoantibodies other than those mentioned above – such as anti-Ro52, anti-PML, and anti-LC1 – in PBC has not been established. In the Polish PBC patient population, these occur at frequencies of 34%, 15%, and 6%, respectively [5].

Some authors have suggested an association with faster disease progression, although this requires further study.

## Differentiation (LoA: 96%)

The differential diagnosis should consider all conditions involving liver dysfunction or cholestasis, but priority should be given to the following liver diseases:
– autoimmune hepatitis,
– sclerosing cholangitis,
– fatty liver disease,
– viral hepatitis,
– drug-induced and toxic liver injury,
– IgG4-related sclerosing cholangitis,
– intrahepatic vascular diseases,
– liver storage diseases (hemochromatosis, Wilson's disease, sarcoidosis, Langerhans cell histiocytosis, hepatic amyloidosis),
– other diseases presenting with cholestasis.

## Assessment of disease severity (LoA: 99%)

The primary clinical symptoms that typically manifest in the advanced stage of PBC are pruritus and progressive fatigue. To objectively assess the severity and progression of pruritus, it is useful to employ the 5-D itch scale. The Numerical Rating Scale (NRS) – a simpler, albeit less precise, tool – can be used to evaluate average and maximum pruritus intensity over the preceding 24 hours on a scale of 0 to 10. A corresponding scale, the NRS-F (Fatigue Numerical Rating Scale), enables assessment and monitoring of fatigue progression [19, 20].

Upon establishing a diagnosis of PBC, it is necessary to assess the disease stage, which serves as a baseline for comparison with the subsequent disease course. This assessment is essential for determining the prognosis and planning further management. Key laboratory markers include ALP and GGT activities, as well as levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, and albumin, along with platelet count and the international normalized ratio (INR) of prothrombin time. Calculating the FIB-4 (fibrosis index 4) and APRI (AST-to-platelet ratio index) scores is also recommended, and patients with cirrhosis should be classified according to the Child-Pugh score.

In addition to a routine liver ultrasound, it is advisable to assess liver stiffness measurement (LSM) using elastography. If necessary for diagnosis or differential diagnosis, a liver biopsy should be considered to allow for histological assessment. Patients diagnosed with cirrhosis due to PBC should undergo upper gastrointestinal endoscopy to screen for esophageal varices. However, according to the Baveno VII criteria, endoscopic assessment may be omitted in patients with an LSM < 20 kPa and a platelet count > 150,000/mm$^3$ [21].

## Goals of PBC treatment (LoA: 100%)

The primary goal of PBC therapy is to halt or at least slow disease progression at the earliest possible stage. This aims to prevent the development of cirrhosis and the need for liver transplantation, thereby helping to prolong life. An additional treatment goal is to improve patients' quality of life by reducing the severity of pruritus and fatigue.

## First-line treatment (LoA: 98%)

Once a diagnosis of PBC is established, ursodeoxycholic acid (UDCA) should be used as first-line therapy at a dose of 13-15 mg/kg daily [4]. There is insufficient evidence to support the use of fenofibrate, obeticholic acid, or budesonide.

## Assessment of treatment outcomes (LoA: 97%)

Treatment efficacy should be assessed between 6 and 12 months after the initiation of therapy by analyzing the previously mentioned laboratory markers, with particular attention paid to ALP activity and bilirubin levels, as these directly influence decisions regarding further management. Changes in the severity of pruritus and fatigue – objectively measured using the 5-D scale, NRS, and NRS-F – often serve as a key factor motivating patients to continue treatment [22]. Given the primary limitation of liver biopsy – its invasive nature, which precludes frequent repetition – monitoring changes in LSM, FIB-4, or APRI has become a common approach for tracking disease progression [22]. To facilitate the early detection of neoplastic changes, it is advisable to perform liver ultrasound and measure CA 19-9 and AFP levels when assessing the efficacy of PBC treatment. For patients with advanced PBC, it is recommended to determine prognosis using the GLOBE or UK-PBC scores, which can be calculated *via* publicly available websites [23-25].

## Effective treatment (LoA: 99%)

First-line therapy is considered effective if, 6-12 months after initiation, bilirubin levels normal-

ize and ALP activity decreases to below 1.67 times the upper limit of normal (ULN). If baseline ALP activity was between the ULN and 1.5 times the ULN, therapy may be considered effective once ALP activity normalizes [22, 26].

## Management following successful first-line therapy (LoA: 99%)

Successful UDCA treatment justifies continuing therapy at an optimal dose of 13-15 mg/kg daily, with monitoring of ALP, GGT, ALT, and AST activity, bilirubin levels, and platelet counts every 6 months. Liver stiffness measurement and ultrasound (USG) should be performed every 12 months; however, once cirrhosis is diagnosed, USG should be performed every 6 months. In patients with early-stage disease (LSM < 9 kPa) and no disease progression, monitoring with the aforementioned markers should be performed annually. If long-term follow-up indicates a stable disease course, check-ups may be performed at longer intervals – though no less frequently than every 2 years – to maintain the status of continued treatment.

During follow-up assessments for PBC, it is advisable to monitor and treat lipid disorders, osteoporosis, and metabolic syndrome, and to provide fat-soluble vitamin supplementation when indicated. At the same time, the need for screening for other autoimmune diseases should be kept in mind.

## Management following unsuccessful first-line therapy (LoA: 100%)

If UDCA monotherapy is ineffective, treatment should be continued in combination with one of the peroxisome proliferator-activated receptor (PPAR) agonists:
– Elafibranor (Iqirvo), 80 mg daily [27, 28],
– Seladelpar (Lyvdelzi), 10 mg daily [29, 30].

Patients with cirrhosis and a history of decompensation and/or portal hypertension should not receive PPAR agonists; they should be promptly referred for liver transplantation.

## Management of UDCA intolerance (LoA: 100%)

If adverse reactions occur during UDCA treatment that prevent continuation of therapy, UDCA should be replaced immediately with a PPAR agonist, administered as monotherapy at the doses specified above. Patients with a history of decompensation and/or portal hypertension should not receive PPAR agonists; they should be immediately referred for liver transplantation.

## Management of intolerance or lack of efficacy of second-line therapy (LoA: 96%)

As with first-line therapy, the efficacy of second-line therapy should be assessed between 6 and 12 months after initiation. If treatment is found to be ineffective, the PPAR agonist should be switched to another, and treatment should be continued in combination with UDCA, provided it is tolerated.

## Antipruritic treatment (LoA: 96%)

For pruritus associated with PBC, particularly when mild, topical emollients may be effective. However, the primary method for alleviating pruritus should be the oral administration of cholestyramine at a dose of 4-16 g daily. If this proves ineffective despite the maximum dose, rifampicin at 150-300 mg daily may be considered. Inhibitors of ileal bile acid transporters (IBATs) may emerge as a future therapy for PBC-associated pruritus. Among the agents in this class, the introduction of linerixibat is expected in the near future (it received a positive EMA opinion on July 26, 2026); meanwhile, odevixibat and maralixibat – despite demonstrating efficacy in other cholestatic diseases – have not yet been authorized for the treatment of pruritus in PBC.

## Liver transplantation (LoA: 100%)

Liver transplantation should be considered for patients with advanced liver disease due to PBC, particularly in the presence of:
– LSM values exceeding 20 kPa, especially when accompanied by a platelet count of ≤ 150,000/mm$^3$ – which indicates a higher likelihood of clinically significant portal hypertension [31],
– an unfavorable prognosis regarding disease progression based on GLOBE or UK-PBC score calculations,
– episodes of decompensation or signs of portal hypertension,
– Child-Pugh class B or C status,
– a diagnosis of hepatocellular carcinoma or bile duct cancer,
– persistently elevated bilirubin levels (> 3 mg/dl),
– intractable, prolonged, and treatment-resistant pruritus with an NRS score > 6 (mean or maximum) or a 5-D score > 20.

Identification of any of the above conditions warrants referral to a liver transplant center.

## Post-liver transplant therapy (LoA: 100%)

Following liver transplantation, patients with PBC are managed according to immunosuppression protocols consistent with transplant standards and recommendations. However, due to the risk of disease recurrence, they should also continue to receive UDCA at a dose of 13-15 mg/kg daily.

## Autoimmune hepatitis in a patient with PBC (LoA: 98%)

A suspicion of autoimmune hepatitis (AIH) in patients with PBC arises upon the detection of ANA or other AIH-associated autoantibodies, alongside disproportionately high aminotransferase activity despite a reduction in ALP activity during PBC therapy. Diagnosis of the AIH/PBC overlap syndrome requires histological confirmation. Measuring immunoglobulin M and G levels can be useful in the differential diagnosis. Once the diagnosis of AIH/PBC overlap syndrome is established, initial management should prioritize immunosuppressive therapy in accordance with AIH guidelines, alongside appropriate management of PBC.

## Management during pregnancy (LoA: 100%)

In pregnant patients with PBC, there are no contraindications to the use of UDCA at a dose of 13-15 mg/kg daily, or to the use of cholestyramine as an additional treatment for pruritus. Rifampicin may be considered only in the third trimester. PPAR agonists should not be used.

## Disclosures

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