Primary Biliary Cirrhosis Diagnostic Panel, Comprehensive

**Test Code:** 19876(X)

**Specimen Requirements:** 4.5 mL refrigerated serum; 1.6 mL minimum

**CPT Codes*: 83516, 86038, 86235 (x2), 86255, 86376 (x2)

### CLINICAL USE
- Diagnose primary biliary cirrhosis (PBC)
- Differentiate PBC from autoimmune hepatitis (AIH)

### CLINICAL BACKGROUND
PBC is a chronic cholestatic, autoimmune disorder characterized by progressive destruction of small intrahepatic bile ducts and portal inflammation. The loss of bile ducts leads to decreased bile secretion and decreased liver function. The inflammation within the liver can result in fibrosis, cirrhosis, and eventual liver failure. PBC is most common in middle-aged women and may be associated with nonhepatic autoimmune diseases such as thyroiditis and Sjögren syndrome. Early diagnosis of PBC and initiation of therapy are necessary to slow disease progression and manage associated complications such as osteoporosis and fat-soluble vitamin deficiency.

Patients with PBC may present with fatigue and pruritus, but most are asymptomatic and identified by elevated alkaline phosphatase (ALP) levels (≥1.5 times the upper limit of the reference range). Presentation may also include symptoms of nonhepatic autoimmune diseases (eg, thyroid dysfunction, dry eyes and mouth). Diagnosis of PBC proceeds with confirmation of the hepatic origin of ALP (eg, elevated alanine aminotransferase [ALT]), testing for mitochondrial antibodies, and noninvasive imaging to exclude biliary obstruction. The combination of a cholestatic pattern of liver function tests (ie, increased ALP and ALT) and a positive mitochondrial antibody result is sufficient for diagnosis of PBC according to guidelines. Liver biopsy demonstrating the presence of asymmetric destruction of interlobular and septal bile ducts may also be recommended. Approximately 5% to 10% of PBC patients do not have mitochondrial antibodies; thus, liver biopsy and tests for antinuclear antibodies (ANAs), smooth muscle antibodies, and immunoglobulins are recommended to confirm or rule out PBC in mitochondrial antibody-negative patients. Liver biopsy and these latter tests are also useful to differentiate PBC from AIH, another autoimmune disease associated with chronic liver disease (see Interpretive Information below). Nearly all patients with PBC have elevated immunoglobulin M (IgM) levels, whereas AIH is characterized by elevated IgG levels.

The PBC Diagnostic Panel includes an immunofluorescence assay for mitochondrial antibodies; tests that can help differentiate PBC from AIH (ie, actin [smooth muscle] antibody, ANAs, and liver/ kidney microsome-1 antibody [LKM-1]); and tests to detect two of the most common nonhepatic autoimmune diseases associated with PBC (ie, SS-A and SS-B for Sjögren syndrome and thyroid peroxidase [TPO] antibody for autoimmune thyroid disease). Although data are often inconsistent across studies, comorbidity of PBC is 10% to 17% with Sjögren syndrome and ≈10% with thyroid disease.

### INDIVIDUALS SUITABLE FOR TESTING
- Individuals with suspected cholestatic liver disease
- Individuals with chronic liver disease of unknown cause

### METHOD
- Mitochondrial antibody screen: immunofluorescence assay (IFA) with reflex to titer when screen is positive (at additional charge [CPT code 86256])
- ANA screen: IFA with reflex to titer and pattern when screen is positive (at additional charge [CPT code 86039])
- Actin (smooth muscle) antibody (IgG): enzyme-linked immunosorbent assay (ELISA)

### Table. Antibody Frequencies (%) Observed in PBC and AIH

<table>
<thead>
<tr>
<th></th>
<th>Mitochondrial Antibody</th>
<th>ANA</th>
<th>Actin Antibody</th>
<th>LKM-1 Antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBC</td>
<td>85</td>
<td>50</td>
<td>30</td>
<td>--</td>
</tr>
<tr>
<td>AIH type 1</td>
<td>--</td>
<td>67</td>
<td>72</td>
<td>--</td>
</tr>
<tr>
<td>AIH type 2</td>
<td>--</td>
<td>--</td>
<td>72</td>
<td>100</td>
</tr>
</tbody>
</table>

PBC, primary biliary cirrhosis; AIH, autoimmune hepatitis; ANA, antinuclear antibody; LKM, liver kidney microsome.

* Typically absent.

b Data are from one study, n = 22.
Antibodies to SS-A and SS-B are present in greater than 90% of patients with Hashimoto thyroiditis and up to 90% of patients with Graves disease. Antibodies to SS-A and SS-B are not disease-specific but are present in up to 95% and 87%, respectively, of patients with Sjögren syndrome.

The presence of immune complexes or other immunoglobulin aggregates in the specimen may lead to false-positive ELISA results. Antibody results should be interpreted in conjunction with other laboratory and clinical findings in patients with suspected PBC.

**INTERPRETIVE INFORMATION**

Antibody patterns associated with PBC and AIH types 1 and 2 are shown in the Table. Detection of mitochondrial antibodies, typically absent in AIH, has a sensitivity of 85% and specificity of 98% for PBC. Patients with negative mitochondrial antibody results and histologically proven PBC tend to have higher levels of ANAs and/or smooth muscle antibodies and lower levels of IgM than patients with mitochondrial antibody–positive PBC. The clinical course of the disease is not associated with mitochondrial antibody status.

ANA results have prognostic value in patients with PBC; in both symptomatic and asymptomatic PBC patients, the presence of ANAs is associated with a shorter time to liver failure.

Positive results for TPO antibody are suggestive of thyroid disease; TPO antibody is present in greater than 90% of patients with Hashimoto thyroiditis and up to 90% of patients with Graves disease.

*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.*

**References**