

## Test Highlights

### Clinical Use

- Assess prognosis and need for aggressive therapy in patients with chronic lymphocytic leukemia (CLL)

### Clinical Background

CLL has a highly variable course. Some patients survive for decades without needing treatment, whereas others progress rapidly and require aggressive therapy within several years after diagnosis. Predicting which patients will progress rapidly can help determine the need for close follow-up and may hold potential for risk-adapted treatment strategies.

The most established predictor of disease progression is lack of mutation in the immunoglobulin heavy chain variable region (IgVH) in neoplastic cells. However, because IgVH mutation testing is not widely available, several surrogate markers have been investigated. To date, the most effective such marker is expression of zeta-associated protein 70 (ZAP-70), a 70-kD member of the Syk family of protein tyrosine kinases. ZAP-70 is expressed primarily in T-cells and natural killer (NK) cells and is critical for signal transduction following T-cell receptor engagement. In CLL B-cells, elevated ZAP-70 expression appears to predict the need for therapy as effectively as IgVH mutation status. Although IgVH mutation status is strongly correlated with ZAP-70 expression, the combination of the 2 markers may provide greater prognostic value than either marker alone.

### Method

This 4-color flow cytometry assay utilizes ZAP-70, CD3, CD19, and CD45 monoclonal antibodies. The fluorescently labeled lymphocyte population is selected by CD45 versus side scatter gating. The percentages of CD3 (B-cell)-positive and CD19 (T-cell)-positive lymphocytes expressing ZAP-70 are reported; samples in which >15% of the B-cell population expresses ZAP-70 are considered positive.

CPT codes\*: 88184, 88185

### Interpretive Information

Positive ZAP-70 results predict an aggressive disease course. Patients with positive results require close follow up to detect changes in clinical status. Negative results predict a more indolent disease course.

Testing for IgVH mutation status, available through Quest Diagnostics, may provide additional prognostic information.

### Specimen Requirements

Submit 5 mL room temperature EDTA (lavender-top tube) whole blood (1 mL minimum). Green-top and yellow-top tubes are also acceptable.

Alternatively, submit 0.5 to 3 mL bone marrow in EDTA or heparin.

Samples must be assayed within 96 hours of collection.

*\*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 payor being billed.*

*This test was developed and its performance characteristics determined by Quest Diagnostics Nichols Institute. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. Performance characteristics refer to the analytical performance of the test.*

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**Company Name**

**Address 1**

**Address 2**

**CSZ**

**Phone 1 and Phone 2**

