

# Diagnostic Tests

## *What Physicians Need to Know*

### Lumipulse G $\beta$ -Amyloid Ratio Test for the Diagnosis of Alzheimer Disease

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**The Lumipulse G**  $\beta$ -Amyloid Ratio assay is a cerebrospinal fluid (CSF) test used to assist in the diagnosis of Alzheimer disease in patients 55 years or older with cognitive impairment. In May 2022, the U.S. Food and Drug Administration authorized the test for marketing.<sup>1</sup> Lumipulse G is an automated system for bead-based immunoassays that measure biomarkers for Alzheimer disease, including amyloid  $\beta$  ( $A\beta$ )1-42, total tau, phosphorylated tau, and the  $A\beta$ 1-42: $A\beta$ 1-40 ratio.<sup>2</sup> These proteins can accumulate to form amyloid plaques, which may be associated with Alzheimer disease.

Amyloid plaque formation decreases the  $A\beta$ 1-42: $A\beta$ 1-40 ratio; thus, a low ratio supports the diagnosis of Alzheimer disease.<sup>3</sup> In three independent cohorts of older adults with cognitive symptoms in Canada, Italy, and the Czech Republic, a cutoff value of 0.072 was established based on correlation with amyloid plaques detected on positron emission tomography (PET) scans and other immunoassay tests.<sup>4-6</sup>

#### Accuracy

In an unpublished diagnostic accuracy study reported in a U.S. Food and Drug Administration press release, 292 CSF samples from the Alzheimer's Disease Neuroimaging Initiative were tested using the Lumipulse G  $\beta$ -Amyloid Ratio assay and then compared with the results of an amyloid PET scan. The study showed that 97% of individuals with positive Lumipulse G test results had amyloid plaques on the PET scan, and 84% of individuals with negative test results had negative findings on the PET scan.<sup>1</sup> A published study comparing the Lumipulse G test with other immunoassays found the test had a sensitivity and specificity for amyloid plaques of 92% and 71%, respectively. The Lumipulse G test also showed high validity and reproducibility compared

Test	Indication	Population	Cost*
Lumipulse G $\beta$ -Amyloid Ratio	Evaluation for Alzheimer disease	Patients 55 years or older with cognitive impairment	Unknown

\*—The test price is not available from the manufacturer (Fujirebio) at this time.

with other immunoassay methods in a clinical laboratory setting.<sup>6</sup> However, research studies comparing patients who have Alzheimer disease with unaffected control groups often produce higher accuracy estimates than would be obtained in real-world clinical settings.

#### Benefit

Based on the correlation of the Lumipulse G  $\beta$ -Amyloid Ratio test with the presence of amyloid plaques in the brains of patients with Alzheimer disease, this test may decrease the time to diagnosis and help initiate earlier treatment. It may also reduce the need for PET scans, which are costly and increase patient exposure to radiation.<sup>2,5</sup> A multicenter U.S. study of 16,000 patients 65 years and older found that amyloid PET scan results often change the clinical management of patients with mild cognitive impairment and dementia of uncertain etiology.<sup>7</sup> However, it is uncertain if earlier detection and management of Alzheimer disease improves clinical outcomes.

#### Harms

Although a lumbar puncture is considered a low-risk procedure, it can cause minor to major adverse effects such as headaches, bleeding, infections, and rare brain herniations.<sup>8</sup> The requirement to obtain a CSF sample may also limit the availability of this test. False-positive results could lead to ineffective treatment and psychological distress for patients and family members. False-negative results could potentially worsen health outcomes by delaying diagnosis and appropriate treatment.<sup>1</sup>

#### Cost

The cost of the Lumipulse G  $\beta$ -Amyloid Ratio test is not available from the manufacturer. It is unknown whether

This series is coordinated by Natasha J. Pyzocha, DO, contributing editor.

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**Author disclosure:** No relevant financial relationships.

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Medicare, Medicaid, or private insurance covers the cost of this test. The cost of the lumbar puncture procedure ranges from \$800 to \$1,500<sup>9</sup> and may be covered by Medicare in certain circumstances.

### Bottom Line

The Lumipulse G  $\beta$ -Amyloid Ratio test is used to assist physicians in diagnosing Alzheimer disease in older patients with cognitive impairment. In research studies, the test was reasonably accurate in predicting the presence of amyloid plaques on PET scans. However, the need for a lumbar puncture makes it less convenient and available than a blood test. Further research is needed to determine if the Lumipulse G test improves diagnostic accuracy, management, and clinical outcomes for patients with Alzheimer disease.

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