Test Definition: C2NAD

PrecivityAD, Plasma

Overview

Useful For

Assisting in the evaluation of adult patients, aged 55 years and older, with signs or symptoms of mild cognitive impairment or dementia who are being assessed for Alzheimer disease and other causes of cognitive decline

This is **not intended for** patients younger than 55 years, or for use as a screening test in patients without signs or symptoms of cognitive impairment, or for serial testing for assessment of longitudinal changes.

Highlights

The PrecivityAD test identifies whether a patient with signs or symptoms of cognitive decline is likely to have amyloid plaques in the brain, a pathological hallmark of Alzheimer disease.

This blood test measures amyloid beta (Abeta) 42/40 ratio and apolipoprotein E isoforms E2, E3, and E4. Individual Abeta42 and Abeta40 concentrations are not reported.

Method Name

Immunoprecipitation/Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Plasma

Ordering Guidance

This blood test is intended for use in patients aged 55 and older with signs or symptoms of mild cognitive impairment or dementia who are undergoing evaluation for Alzheimer disease or other forms of cognitive decline.

Shipping Instructions

1. Specimen should be shipped frozen on dry ice
2. Place labeled aliquot tube inside a larger tube or vial for transport.

Specimen Required

Supplies: Screw cap micro tube, 2 mL, PCR Performance Tested, Low protein-binding (T983)
Collection Container/Tube: 10 mL Purple top (K EDTA)
Submission Container/Tube: 2-mL screw cap micro tubes
Specimen Volume: 1.5 mL
Collection Instructions:
1. Centrifuge within two hours of collection.

2. Aliquot plasma into a 2 mL micro tube.
3. Freeze plasma (no longer than 2 hours after collection) at -20 degrees C or below.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject
Outside of age range Specimen collected outside of testing range (too long in storage before arrival to testing facility) Insufficient volume Incorrect labeling	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Frozen		

Clinical & Interpretive

Clinical Information

Alzheimer disease (AD) is defined pathologically by the presence of amyloid plaques and neurofibrillary tangles in the brain. Clinical characteristics include gradual onset of mild cognitive impairment (MCI), behavioral changes such as apathy, withdrawal, or agitation, and disease progression to middle and later stage dementia.(1,2) Currently, no test detects AD with 100% accuracy; definitive diagnosis occurs at brain autopsy.

MCI impacts 12% to 18% of people in the United States over age 60 and is often an initial clinical sign of AD.(3) Detection of AD at an early stage, such as at onset of MCI or memory loss, can optimize medical management by providing access to therapies and clinical trials and by allowing for lifestyle changes that prioritize aerobic exercise, quality sleep and a healthy diet. Detection at first signs of MCI is also important for personal or family knowledge and planning, and for

accessing appropriate community support and resources. Exclusion of AD with a high degree of certainty is equally important since MCI can have other etiologies, some of which are treatable.

Amyloid positron emission tomography (PET) scan and cerebrospinal fluid (CSF) testing detect brain amyloid pathology with high sensitivity and specificity in patients with MCI and early dementia.(4,5) Results of these tests are interpreted in the context of the patient's clinical findings and other clinical work-up, as the neuropathological changes associated with AD can be seen in unaffected individuals.(4,5) Highly sensitive and specific blood biomarker testing offers an accessible and less procedurally complex option to amyloid PET scan or CSF testing for assessment of brain amyloid plaques.(6,7)

The PrecivityAD test is an analytically and clinically validated blood test that aids healthcare providers in the diagnosis of AD in patients with MCI and early-stage dementia. This evaluation simultaneously quantifies plasma amyloid beta (Abeta) 42 and 40 (Abeta42 and Abeta40) concentrations and determines the presence of apolipoprotein E (ApoE)-specific peptides (to determine APOE genotype). The test's statistical algorithm combines the Abeta 42/40 ratio, established APOE genotype, and patient age to calculate the likelihood that a patient is positive for the presence of amyloid plaques by amyloid PET scan.(6-8) APOE proteotype/genotype, included in the test results, can aid in decision-making about treatment paths for some patients: In recent clinical trials for amyloid-reducing therapies, the E4 allele showed association with development of amyloid-related imaging abnormalities (ARIA); cerebral edema (ARIA-E); and cerebral microhemorrhages (ARIA-H).(9,10)

Reference Values

Amyloid Probability Score (APS): 0-100
Low (0-35): Consistent with absence of amyloid plaques
Intermediate (36-57)
High (58- 100): Consistent with presence of amyloid plaques

Abeta42/40 Ratio
> or =0.095: Consistent with absence of amyloid plaques

ApoE Proteotype
E2/E2, E2/E3, E2/E4, E3/E3, E3/E4, E4/E4
-E3 is the most common allele.
-E4 allele is associated with increased risk of amyloid plaques.
-E2 allele is associated with lower risk of amyloid plaques.

Interpretation

The Amyloid Probability Score (APS) represents the estimated likelihood from 0 (low likelihood) to 100 (high likelihood) that the patient is currently positive on amyloid positron emission tomography (PET) imaging (presence of amyloid plaques) based on their amyloid beta (Abeta) 42/40 ratio, age, and established *APOE* genotype.

A low APS result (0-35) is consistent with a negative amyloid PET scan result and, thus, a low likelihood of amyloid plaques. Absence of amyloid plaques is inconsistent with an Alzheimer disease diagnosis and indicates other causes of cognitive symptoms should be investigated.

An intermediate APS result (36-57) does not distinguish between the presence or absence of amyloid plaques and indicates further diagnostic evaluation may be needed to assess the underlying causes for the patient's cognitive symptoms.

A high APS result (58-100) is consistent with a positive amyloid PET scan result and, thus, a high likelihood of amyloid plaques. Presence of amyloid plaques is consistent with an Alzheimer disease diagnosis in someone who has cognitive decline, but alone is insufficient for a final diagnosis; clinical presentation and other factors should be considered along with the APS result.

Cautions

This test is not a standalone test; high, intermediate, or low Amyloid Probability Score (APS) values alone neither establish nor rule out a diagnosis of Alzheimer disease (AD).

Test results should be used in conjunction with other diagnostic tools, such as neurological examination, neurobehavioral tests, imaging, and routine laboratory tests.

False-positive and false-negative test results may occur.

This test uses interpretive data that were derived from clinical studies in a predominantly White US population of patients with mild cognitive impairment or early dementia. The extent of the differences in results (if any) based on individuals of other racial and ethnic groups has not yet been firmly established.

Currently, there is insufficient evidence to support serial testing for the assessment of longitudinal changes in biomarkers; therefore, serial testing is not recommended.

Clinical Reference

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3. Alzheimer's Association. Mild Cognitive Impairment (MCI). Accessed June 16, 2023. Available at www.alz.org/alzheimers-dementia/what-is-dementia/related_conditions/mild-cognitive-impairment.
4. Johnson KA, Minoshima S, Bohnen NI, et al. Update on appropriate use criteria for amyloid PET imaging: dementia experts, mild cognitive impairment, and education. Amyloid Imaging Task Force of the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging. Alzheimers Dement. 2013;9(4):e106-e109. doi:10.1016/j.jalz.2013.06.001
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J Prev Alzheimers Dis. 2021;8(4):398-410. doi:10.14283/jpad.2021.41.
10. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. N Engl J Med. 2023;388(1):9-21. doi:10.1056/NEJMoa2212948

Performance

Method Description

Plasma specimens undergo immunoprecipitation followed by liquid chromatography tandem mass spectrometry for the quantification of amyloid beta (Abeta42 and Abeta40) peptide isoform concentrations and the identification of apolipoprotein E (ApoE) peptides corresponding to ApoE2, ApoE3, ApoE4 isoforms. The Amyloid Probability Score (APS) uses a statistical algorithm combining Abeta42/40 ratio, ApoE proteotype (determined by ApoE peptide isoforms), and patient age.(West T, Kirmess KM, Meyer MR, et al. A blood-based diagnostic test incorporating plasma Abeta42/40 ratio, ApoE proteotype, and age accurately identifies brain amyloid status: findings from a multi cohort validity analysis. Mol Neurodegener. 2021;16[1]:30. Published 2021 May 1. doi:10.1186/s13024-021-00451-6; Hu Y, Kirmess KM, Meyer MR, et al. Assessment of a Plasma Amyloid Probability Score to Estimate Amyloid Positron Emission Tomography Findings Among Adults With Cognitive Impairment. JAMA Netw Open. 2022;5[4]:e228392. Published 2022 Apr 1. doi:10.1001/jamanetworkopen.2022.8392)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

13 days post sample receipt from MCL

Specimen Retention Time

60 days

Performing Laboratory Location

C2N Diagnostics LLC

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

C2N Diagnostics has developed and determined the analytical and clinical validity performance characteristics of this

Laboratory Developed Test (LDT). This assay has been validated pursuant to CLIA regulations and is used for clinical purposes. This assay has not been cleared or approved by the FDA.

CPT Code Information

0412U

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
C2NAD	PrecivityAD	Not Provided

Result ID	Test Result Name	Result LOINC® Value
ND2B	Amyloid Probability Score (APS)	Not Provided
ND2C	Interpretation	Not Provided
ND2D	APS Reference Interval	Not Provided
ND2F	Abeta42/40 Ratio	Not Provided
ND2G	Abeta42/40 Ratio Reference Interval	Not Provided
ND2H	Abeta42/40 Ratio Description	Not Provided
ND2I	ApoE Proteotype	Not Provided
ND2J	ApoE Proteotype Reference Interval	Not Provided
ND2K	Test Description	Not Provided
ND2L	Limitations of Test Result	Not Provided
ND2M	Methods and Assay Category	Not Provided
ND2N	References	Not Provided
ND2O	Report Comment	Not Provided
ND2E	Patient Age	Not Provided
ND2P	Performing Site	Not Provided
ND2BF	APS Result	Not Provided