



ACNA Clinical Guidelines: Plasma p-tau217

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1. We welcome the development of plasma biomarkers for the diagnosis of the most common neurodegenerative disorder, Alzheimer's disease (AD).
2. Abnormally elevated levels of Tau phosphorylated at threonine 217 (pTau217) can be used as a marker of Alzheimer's disease pathological and physiological change. It is detectable in the cerebrospinal fluid, and at much lower concentrations in plasma. In this context, it is an early marker of Alzheimer's pathology, which is most-strongly correlated with amyloid-plaque deposition, which increases with age and can be detected in cognitively normal individuals [Jack et al, 2024].

Phosphorylated tau isoforms, especially phosphorylated tau217 (p-tau217), has proven to be an accurate marker of neuropathological Alzheimer's disease, including neuritic plaques and neurofibrillary tangles. Tau protein stabilises microtubules and is hyperphosphorylated at threonine at position 217. This phosphorylation of tau destabilises tau, resulting in its disintegration from the microtubules [?] the

aggregation of hyperphosphorylated tau into neurofibrillary tangles [?] neuronal death. P-tau217 is found also at synapses where there is A β deposition [Gonzalez-Ortiz *et al*, 2023; Pichet Binette *et al*, 2025].

3. P-tau217 has an excellent correlation with amyloid and tau PET findings and with cerebrospinal fluid (CSF) biomarkers [Ashton *et al*, 2024].
4. The USA FDA has granted approval for the Lumipulse p-tau217 / A β 42 ratio, C2N Precivity2 test based on pTau217 phosphorylation percentage, and the Elecsys pTau217 assay. In Australia, the Elecsys pTau217 has been approved by the Therapeutic Goods Administration (TGA) and included in the Australian Register of Therapeutic Goods (ARTG), as part of the diagnostic evaluation of suspected Alzheimer's disease, to rule in or out the presence of amyloid pathology (estimated cost is AU\$350).
5. P-tau217 is considered sensitive and specific for the presence of amyloid pathology as determined by CSF (sensitivity 82-90% and specificity 83-88%) in primary and secondary care using the Lumipulse assay, with area under the curve of 0.93-0.96, [Palmqvist *et al*, *Nat Med*, 2025; Palmqvist *et al*, *Alz & Dem*, 2025(a) & 2025(b)].
6. High diagnostic accuracy does not negate that careful clinical assessment is required for the application to be useful in practice, as positive and negative predictive values for AD pathology is contingent on clinical context and pre-test probability [Therriault *et al*, 2024],

and pTau217 levels in the blood can be influenced by other comorbidities or neurological diseases and may be found in the blood in other clinical circumstances:

- Prion diseases – sporadic and variant Creutzfeldt-Jacob disease [Bentivenga *et al*, 2025; Coysh *et al*, 2026].
- Motor neuron disease [Janelidze *et al*, 2025; Abu-Rumeileh *et al*, 2026].
- Niemann-Pick disease, type C [Gonzalez-Ortiz *et al*, 2024].
- Chronic kidney disease and renal failure can increase p-tau217 [Bornhorst *et al*, 2025].
- Elevated BMI results in lower pTau217 [Yun *et al*, 2026].
- Fasting status has an impact as food intake decreases plasma p-tau217 levels, which may influence concentration by 30% [Schuder *et al*, 2025].

7. Therefore, plasma p-tau217 cannot and should not be used as a sole biomarker for the diagnosis of AD as this will result in diagnostic errors.
8. The diagnosis of Alzheimer's disease must be based on the sound clinical foundations of history and examination, and where an understanding of the patient's amyloid status will inform diagnosis or management, this can be supported by tests including plasma p-tau217.
9. Plasma p-tau217 has a limited role in preclinical disease and is less reliable in those who are asymptomatic and a multimarker approach might help people in the preclinical state [Salvadó *et al*, 2025; Binks & Graff-Radford, 2025]. It might have a use monitoring clinical deterioration [Selma-Gonzalez *et al*, 2025].
10. This test is not recommended for those under 50 years of age or those who have no cognitive symptoms.

11. Reference ranges will depend on local measurements; some assays report a dual cut-point approach to improve the positive and negative predictive value of positive/negative test results, with the consequence of assigning 10-40% of patients an intermediate (or indeterminate) result, which is a range of pTau217 levels where this has limited predictive value for someone's amyloid-PET or CSF AD biomarker status (examples from the MAYO Clinic):

Negative predicts negative amyloid PET; low probability AD neuropathological change.

Intermediate cannot predict presence/absence of Alzheimer pathological change. Amyloid PET scan, CSF A β and tau may be necessary.

Positive consistent with positive amyloid PET scan and consistent with AD neuropathological change. In the correct clinical context this is diagnostic of AD as the explanation for the patients' symptoms.

12. The plasma p-tau217 is not a predictive test for the development of Alzheimer's disease and is not a screening test for those without symptoms. P-tau217 has not been shown to be diagnostic in those without symptoms and this information should be provided to asymptomatic people who are at risk of developing AD [Bellomo & Gaetani, 2026].
13. Much of our current understanding of the diagnostic utility of p-tau217 is based on data from highly selected populations. We recommend validation of this test in culturally and linguistically diverse populations, including Aboriginal and Torres Strait Islander peoples. Validation must occur in tandem with community consultation.

14. We encourage Medicare to add this test to the Medicare Benefits Schedule (MBS) to support earlier diagnosis and care approaches for priority populations, including regional and remote Australians where access to PET or CSF biomarkers may be limited.
15. These Guidelines are a work in progress. As more information comes to hand this Statement will be modified.

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