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DIAGNOSTIC
New medicinal product
9 January 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

NEURACEQ (^{18}F-florbetaben), radiopharmaceutical

Insufficient clinical benefit to justify reimbursement in the detection of β-amyloid neuritic plaque due to the absence of data in the MA population and limited diagnostic performance

Main points

- NEURACEQ has an MA for Positron Emission Tomography (PET) imaging of

  β-amyloid neuritic plaque density in the brains of adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD) and other causes of cognitive impairment.
- There is no direct link between β-amyloid neuritic plaque density and the formal diagnosis, severity or progression of Alzheimer's disease.
- The role in the diagnostic strategy of florbetaben-PET remains to be defined given the clinical performance limitations and the quality of the demonstration.
- There is no direct comparison between florbetaben-PET and assay of Aβ42 or tau proteins in CSF.

Diagnostic strategy

- The only definite diagnosis of Alzheimer's disease is obtained post mortem, following brain autopsy.
- Diagnosis in living patients is a clinical diagnosis based on the presence of cognitive impairment. A biological signature in CSF is mainly necessary in more complex forms of Alzheimer's disease. In 2014, an expert consensus proposed adding the detection of amyloid deposits, via PET imaging, in particular. For cases in which diagnosis is difficult, memory consultations may take place in expert centres, and memory resource and research centres in France (CMRRs).
- **Role of the medicinal product in the diagnostic strategy**

  Considering, in particular:
  - the diagnostic performance limitations of florbetaben-PET;
  - the inclusion in the phase III study of patients with an already established diagnosis of Alzheimer's disease, Lewy body dementia or other forms of dementia, without data on patients for whom the diagnosis is complex and where this test could be useful in view of the medical need;
  - the absence of a direct link between amyloid plaque density and the formal diagnosis, severity or progression of Alzheimer's disease, calling into question the clinical utility of this test,
  - the absence of direct comparison between florbetaben-PET and assay of Aβ42 or tau proteins in CSF,

  the role in the diagnostic strategy of PET imaging following the administration of NEURACEQ remains to be defined in its indication.

Clinical data

A non-randomised, open-label, phase III trial evaluated the sensitivity and specificity of florbetaben (18F)-PET imaging to detect β-amyloid plaque density compared to post-mortem histopathology (standard of truth). The primary combined endpoints, sensitivity and specificity, were evaluated during an interim analysis scheduled in the protocol, without any division of the α risk between the 2 combined endpoints, on the basis of the 32 brains available, of which 31 were subject to post-mortem histopathological analysis. Analysis of the primary combined endpoints was statistically significant, with a sensitivity of florbetaben-PET of 77.4% compared to histopathology (95% CI = [65.4-89.4], above the 60% threshold and a specificity of 94.2% (95% CI = 88.6- 99.8], above the 80% threshold. No statistical analysis was scheduled for the secondary endpoints.

- A French phase IV study analysed the impact of florbetaben-PET imaging on the change of diagnosis of patients assessed for Alzheimer's disease in CMRRs. The statistical methodology for this study only permits a descriptive analysis of the data. Following the performance of florbetaben-PET, the diagnosis changed for 137/205 patients (66.8%, 95% CI = [59.9; 73.2]). Of the 132 patients having had a positive florbetaben-PET imaging test, a change of diagnosis was made for 76/132 patients (57.6%, 95% CI = [48.7; 66.1]). Of the 73 patients having had a negative florbetaben-PET imaging test, a change of diagnosis was made for 61/73 patients (83.6%, 95% CI = [73.0; 91.2]).

Special prescription requirements

- Medicinal product for hospital use only.
- Medicinal product subject to prescription reserved for certain specialists (PRS).
- Radiopharmaceutical medicinal product.

Benefit of the medicinal product

- The actual clinical benefit* of NEURACEQ is insufficient.
- Not approved for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 09 January 2019 (CT-16710) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.