SUMMARY

florbetaben (18F)

NEURACEQ 300 MBq/ml,

solution for injection

First assessment

Adopted by the Inter-Committee on 4 April 2023

The legally binding text is the original French opinion version

Key points

Favourable opinion on reimbursement for Positron Emission Tomography (PET) imaging in the diagnosis of Alzheimer's Disease, with an atypical clinical presentation due to a mixed presentation, including patients with atypical symptoms or an early age of onset (subjects under 65 years of age) and in the following circumstances:

- when the cognitive deficit has been objectively confirmed and the cause of the cognitive disorder remains uncertain after an assessment by a specialist physician and the investigations recommended by the guidelines
- and when a lumbar puncture to detect and assay the biomarkers Aβ42, Tau and phospho-Tau in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results inconsistent with the clinical presentation).

Unfavourable opinion on reimbursement in the other clinical situations of the MA.

Role in the care pathway?

NEURACEQ (florbetaben (18F)) has a role in the care pathway of Alzheimer's Disease, when the current recommendations provide for the performance of a PET in patients with an atypical clinical presentation due to a mixed presentation, including patients with atypical symptoms or an early age of onset (subjects under 65 years of age) and in the following circumstances: when the cognitive deficit has been objectively confirmed and the cause of the cognitive disorder remains uncertain after an assessment by a specialist physician and the investigations recommended by the guidelines and when a lumbar puncture to detect and assay the biomarkers Aβ42, Tau and

phospho-Tau in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results inconsistent with the clinical presentation).

NEURACEQ (florbetaben (18F)) has no role in the other clinical situations of the MA.

Conclusions of the Inter-Committee (TC - CNEDIMTS)

Clinical Benefit

- Alzheimer's Disease (AD) is a severe, disabling neurodegenerative disease of the central nervous system, with considerable family and social repercussions.
- It is a diagnostic medicinal product.
- The efficacy/adverse effect ratio of NEURACEQ (florbetaben (18F) is significant in the diagnosis of Alzheimer's Disease, with an atypical clinical presentation due to a mixed presentation, including patients with atypical symptoms or an early age of onset (subjects under 65 years of age) and in the following circumstances:
  - when the cognitive deficit has been objectively confirmed and the cause of the cognitive disorder remains uncertain after an assessment by a specialist physician and the investigations recommended by the guidelines
  - and when a lumbar puncture to detect and assay the biomarkers Aβ42, Tau and phospho-Tau in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results inconsistent with the clinical presentation).
- There are diagnostic alternatives: the medicinal product VIZAMYL (flutemetamol, (18F)) and assays of biomarkers present in the CSF (Aβ1-42 proteins, total Tau proteins and phosphorylated Tau proteins).
- It is a first-line examination in the diagnosis of Alzheimer's Disease, with an atypical clinical presentation due to a mixed presentation, including patients with atypical symptoms or an early age of onset (subjects under 65 years of age) and in the following circumstances:
  - when the cognitive deficit has been objectively confirmed and the cause of the cognitive disorder remains uncertain after an assessment by a specialist physician and the investigations recommended by the guidelines
  - and when a lumbar puncture to detect and assay the biomarkers Aβ42, Tau and phospho-Tau in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results inconsistent with the clinical presentation).

  NEURACEQ (florbetaben (18F)) has no role in the other clinical situations of the MA.

➔ Public health benefit

In view of:

- the gravity and high incidence of Alzheimer's Disease,
- the medical need identified to optimise diagnostic techniques in Alzheimer's Disease in order to offer patients appropriate care,
- the absence of proven additional impact on mortality, morbidity or quality of life compared to the available alternatives,
- the absence of an additional expected impact on the care pathway and /or life course

NEURACEQ (florbetaben (18F)) is not liable to have an additional impact on public health.

In view of all of these elements, the Inter-Committee considers that the clinical benefit provided by NEURACEQ (florbetaben (18F)), solution for injection is:

- **significant for Positron Emission Tomography (PET) imaging in the diagnosis of Alzheimer's Disease, with an atypical clinical presentation due to a mixed presentation, including patients with atypical symptoms or an early age of onset (subjects under 65 years of age) and in the following circumstances:**
  - **when the cognitive deficit has been objectively confirmed and the cause of the cognitive disorder remains uncertain after an assessment by a specialist physician and the investigations recommended by the guidelines**
  - **and when a lumbar puncture to detect and assay the biomarkers Aβ42, Tau and phospho-Tau in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results inconsistent with the clinical presentation).**
- **insufficient to justify coverage by national solidarity schemes, in the other clinical situations of the MA.**

The Inter-Committee gives a favourable opinion on the inclusion of NEURACEQ 300 MBq/ml (florbetaben (18F)), solution for injection on the list of medicinal products approved for the use of communities solely for Positron Emission Tomography (PET) imaging in the diagnosis of Alzheimer's Disease, with an atypical clinical presentation due to a mixed presentation, including patients with atypical symptoms or an early age of onset (subjects under 65 years of age) and in the following circumstances:

- **when the cognitive deficit has been objectively confirmed and the cause of the cognitive disorder remains uncertain after an assessment by a specialist physician and the investigations recommended by the guidelines**
- **and when a lumbar puncture to detect and assay the biomarkers Aβ42, Tau and phospho-Tau in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results inconsistent with the clinical presentation).**

The Inter-Committee gives an unfavourable opinion on inclusion on the list of medicinal products approved for the use of communities in the other clinical situations of the MA.

Clinical Added Value

In view of:

- **the data assessed during the initial listing application which reported diagnostic performances for florbetaben-PET compared to post-mortem histopathology in patients with an established diagnosis of Alzheimer's Disease, Lewy Body Dementia or other dementia, with an average age of 74 years, in a phase III study with:**
  - **results with a sensitivity of 77.4% and a specificity of 94.2% in an intermediate analysis provided for a priori in the protocol in the first 31 patients (main analysis conducted by visual assessment, by cortical region),**
  - **the additional results of a post-hoc analysis not provided for a priori in the protocol in a larger group of 74 patients (visual assessment, by patient) with a sensitivity of 97.9% and a specificity of 88.9%,**
- **new data derived from the literature some of which deal with patients with a complex diagnosis (early atypical forms, with focal atrophy, and rapid progression) and which reported data for NEURACEQ (florbetaben (18F)) on the impact on management, institutionalisation and mortality with however associated limitations (data all descriptive without formalised statistical comparisons, no randomisation, or transposability to French practice...),**
- **new data suggesting a concordance between the amyloid florbetaben (18F) PET and that of flutemetamol (18F),**
- **new data suggesting a correlation between florbetaben (18F) PET and some CSF biomarkers without however a compelling demonstration of any advantage in terms of diagnostic performance compared to the detection and assay of CSF biomarkers (Aβ42, Tau and phospho-Tau) performed after lumbar puncture and compared to VIZAMYL (flutemetamol (18F)),**

The Inter-Committee considers that NEURACEQ 300 MBq/ml (florbetaben (18F)), solution for injection provides no clinical added value (CAV V) in the diagnostic strategy of Alzheimer's Disease.