HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
AND
NATIONAL COMMITTEE FOR THE EVALUATION OF MEDICAL DEVICES AND HEALTH TECHNOLOGIES

HAVING MET IN APPLICATION OF ARTICLE L. 161-41 OF THE FRENCH SOCIAL SECURITY CODE

SUMMARY
08 JUNE 2022

The legally binding text is the original French opinion version

flutemetamol (18F)
VIZAMYL 400 MBq/mL solution for injection
First assessment

Key points

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

- when the cognitive impairment has been objectively confirmed and the cause of the cognitive disorder remains uncertain following assessment by a specialised physician and the investigations recommended by the guidelines

- and when the performance of a lumbar puncture to detect and assay Aβ42, Tau and phosphoTau biomarkers in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results not consistent with the clinical presentation).

Unfavourable opinion for reimbursement in the other clinical situations.

What therapeutic improvement?

No clinical added value in the diagnostic strategy for Alzheimer’s disease.

Role in the diagnostic pathway?

A diagnosis of Alzheimer's disease is made within the framework of a multidisciplinary approach. It is based, first of all, on the presence of a cognitive impairment (for example, hippocampal amnestic syndrome). In 2018, an expert consensus proposed a graduated and personalised strategy, with detection in the primary care setting, aetiological diagnosis based on a specialised consultation (geriatric, neurology, memory) supplemented by a brain MRI and first-line blood tests enabling a probable diagnosis of Alzheimer’s and related diseases. For atypical cases (mild cognitive impairment, young patient, rapid cognitive impairment, focal atrophy syndrome), lesion biomarkers, particularly in the cerebrospinal fluid (Aβ42 amyloid peptide and Tau proteins) or PET may be used. In the context of mild cognitive impairment, the consensus recommends that patients seeking a more precise diagnosis should have access to improved diagnostic accuracy via lesion markers from cerebrospinal fluid or PET scans.

Despite the efforts made during the successive neurodegenerative disease plans, it is considered that half of all Alzheimer's disease patients are not diagnosed currently. There are many reasons for this, but according to expert opinion, the most important could be a lack of detection in the primary care setting (general practitioners). The 2014-2019 neurodegenerative diseases plan specifies “the benefit of a proper diagnosis, even when there is no treatment, [in order to be able to adapt] the care pathway and support methods to preserve the patient's quality of life”.

Role of the medicinal product in the care pathway:

VIZAMYL (flutemetamol (18F)) has a role in the diagnostic strategy for Alzheimer’s disease, when the current guidelines schedule the performance of PET in patients with an atypical clinical presentation due to mixed presentation, including patients with an atypical form in terms of symptoms or early age of onset (subjects under 65 years of age) and in the following circumstances: when the cognitive impairment has been objectively confirmed and the cause of the cognitive disorder remains uncertain following assessment by a specialised physician and the investigations recommended by the guidelines and when the performance of a lumbar puncture to detect and assay Aβ42, Tau and phosphoTau biomarkers in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results not consistent with the clinical presentation).

JOINT COMMITTEE CONCLUSIONS

Considering all of this information and further to debate and voting, the Joint Committee considers:

Clinical benefit

◗ Alzheimer's disease (AD) is a severe and debilitating neurodegenerative disease of the central nervous system with significant family and social repercussions.

◗ The proprietary medicinal product VIZAMYL (flutemetamol (18F)) is a medicinal product for diagnostic use.

◗ Considering the absence of studies in patients with an atypical clinical presentation of Alzheimer's disease, raising the question of the transposability of the results to routine practice, the available data not enabling the questions raised concerning the role of a test of this type offered in routine practice in the absence of a treatment modifying the disease course, despite its potential value in a clinical research context, the absence of specific data in patients for whom the diagnosis is complex and where this test could be of benefit in view of the medical need, particularly in early-onset forms (under 65 years of age), atypical forms with focal atrophy, and rapidly progressing forms, and the correlation suggested between PET-flutemetamol (18F) and CSF biomarkers, its efficacy/adverse effects ratio is low.

◗ There are alternative diagnostic methods, in particular assay of biomarkers in CSF (Aβ1-42 proteins, total Tau proteins and phosphorylated Tau proteins)

◗ It is a first-line test when a lumbar puncture to detect and assay Aβ42, Tau and phosphoTau biomarkers in the CSF is contraindicated, cannot be performed or has provided inconclusive results.

Public health benefit

Considering:
- the seriousness and high incidence of Alzheimer's disease,
- the identified medical need to optimise diagnostic methods in Alzheimer's disease in order to offer patients appropriate care,
- the lack of demonstrated additional impact on mortality, morbidity or quality of life compared to the diagnostic methods available,
- the lack of expected additional impact on the care and/or life pathway,

VIZAMYL (flutemetamol (18F)) is unlikely to have an additional impact on public health.

Considering all these elements, the Joint Committee deems that the clinical benefit of VIZAMYL (flutemetamol (18F)) is:

- LOW for Positron Emission Tomography (PET) imaging in the diagnosis of Alzheimer's disease, with an atypical clinical presentation due to mixed presentation, including patients with an atypical form in terms of symptoms or early age of onset (subjects under 65 years of age) and in the following circumstances:

- when the cognitive impairment has been objectively confirmed and the cause of the cognitive disorder remains uncertain following assessment by a specialised physician and the investigations recommended by the guidelines

- and when the performance of a lumbar puncture to detect and assay Aβ42, Tau and phosphoTau biomarkers in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results not consistent with the clinical presentation).

- INSUFFICIENT to justify its public funding cover in all other clinical situations.

The Joint Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the subpopulation of the

indication " for Positron Emission Tomography (PET) imaging in the diagnosis of Alzheimer's disease, with an atypical clinical presentation due to mixed presentation, including patients with an atypical form in terms of symptoms or early age of onset (subjects under 65 years of age) and in the following circumstances:
- when the cognitive impairment has been objectively confirmed and the cause of the cognitive disorder remains uncertain following assessment by a specialised physician and the investigations recommended by the guidelines
- and when the performance of a lumbar puncture to detect and assay Aβ42, Tau and phosphoTau biomarkers in the CSF is contraindicated, cannot be performed or has provided inconclusive results (equivocal results that cannot be interpreted, results not consistent with the clinical presentation)."

The Joint Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the other clinical situations.

Clinical Added Value

Considering the suggested correlation between PET-flutemetamol (18F) and CSF biomarkers, which is nonetheless variable between studies, between the tests used for the assay and depending on the biomarker ratios, but the absence of conclusive evidence provided by VIZAMYL (flutemetamol (18F)) concerning a potential advantage in terms of diagnostic performance compared to detection and assay of biomarkers in CSF (Aβ42, Tau and phosphoTau) conducted after lumbar puncture, **VIZAMYL (flutemetamol (18F)) provides no clinical added value (CAV V)** in the diagnostic strategy for Alzheimer's disease.