Summary of the Risk Management Plan (RMP) for Vizamyl (flutemetamol $^{18}$F)

Version 2

December 2019

Disclaimer:

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine’s safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of Vizamyl is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the “Arzneimittelinformation” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Vizamyl in Switzerland is the "Arzneimittelinformation" (see www. Swissmedicinfo.ch) approved and authorized by Swissmedic. GE Healthcare AG is fully responsible for the accuracy and correctness of the content of the here published summary RMP of Vizamyl.
Summary of the risk management plan (RMP) for Vizamyl (flutemetamol 18F)

This is a summary of the risk management plan (RMP) for Vizamyl, which details the measures to be taken in order to ensure that Vizamyl is used as safely as possible. The reference document which is valid and relevant for the effective and safe use of Vizamyl in Switzerland is the “Arzneimittelinformation” (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

Overview of disease epidemiology

Vizamyl is a medicine used to help diagnose dementia. Alzheimer’s disease is the most common type of dementia, which is characterised by symptoms such as memory loss, mood changes, and problems with communication and reasoning. These symptoms worsen over time and affected individuals eventually require full support to complete simple daily tasks. The risk of developing Alzheimer’s disease and other dementias increases steadily with age, and women are at greater risk of developing the disease than men. In Europe it is estimated that in 2006 over 6 million people had dementia, but as people live longer, this number will increase.

Summary of treatment benefits

Vizamyl is a ‘diagnostic imaging agent’ that contains the active substance flutemetamol 18F. It works by attaching to deposits (plaques) of beta-amyloid if they are present in the brain and emitting low amounts of radiation. This allows plaques to be detected using a type of brain scan known as PET (positron emission tomography). These beta-amyloid plaques are typically seen in the brain of people with Alzheimer’s disease; absence of plaques can help Healthcare Professionals rule out the condition, while their presence may help support a diagnosis of Alzheimer’s disease.

Vizamyl was investigated in one main study in 176 patients nearing the end of their lives who had consented to autopsies when they died, in order to prove conclusively whether or not they had significant amounts of β-amyloid plaques in their brain. At the end of the study the brain autopsies of 68 patients were evaluated. When the results of the autopsies were compared with the PET scans interpreted by skilled readers, the scans were shown to have a sensitivity of between 81 and 93%. This means that the PET scans correctly identified as positive between 81 and 93% of the patients who had significant amounts of plaques in their brain.

A later re-analysis looked again at data from the original 68 patients together with results from others who had died after the end of the original study, making a total of 106 patients. In this re-analysis most readers could interpret the scans with a sensitivity of around 91% (91% of patients who had plaques were identified) and a specificity of 90% (almost all patients without plaques were correctly rated as negative).

Unknowns relating to treatment benefits

It is not known whether differences in patients’ race, age or gender would affect the interpretation of Vizamyl PET brain scans, but based on the studies carried out to assess Vizamyl’s effectiveness there is no evidence to suggest this.
Summary of safety concerns (Important identified risk, important potential risk and important missing information)

Important identified risks

None

Important potential risks

<table>
<thead>
<tr>
<th>Risk</th>
<th>What is known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inaccurate interpretation of Vizamyl PET scans</td>
<td>Although the rate of inaccurate interpretation of Vizamyl PET scans in the clinical studies was found to be low, there is a potential risk that the doctor could misinterpret the images. Interpretation errors may lead to subsequent inappropriate treatment strategies for patients. An educational training programme for Healthcare Professionals reading Vizamyl scans to minimise this risk will be implemented upon approval of the Swiss Marketing Authorisation.</td>
</tr>
<tr>
<td>Lack of information on off-label use</td>
<td>Vizamyl is indicated for diagnostic use in adult patients with symptoms of impaired brain function who are being investigated for Alzheimer’s disease and other dementias. The safety and effectiveness of Vizamyl in other populations (off-label) has not been studied, including in patients at increased risk of Alzheimer’s disease but who do not have symptoms.</td>
</tr>
</tbody>
</table>

Missing information

None

Summary of risk minimisation measures by safety concern

All medicines have a “Arzneimittelinformation” (see www.swissmedic.ch) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. The measures listed in these documents are known as ‘routine risk minimisation measures’.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures).

These additional risk minimisation measures are for the following risks:

Inaccurate interpretation of Vizamyl PET scans

<table>
<thead>
<tr>
<th>Risk minimisation measure: Healthcare professional educational programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective and rationale: Healthcare Professionals reading the scans must be specifically trained in interpreting the images from PET scans with Vizamyl, in order to avoid incorrect interpretation of images, which may lead to subsequent inappropriate treatment of patients.</td>
</tr>
<tr>
<td>Description: Educational training to be provided to Healthcare Professionals who will be tested on reading Vizamyl PET scans.</td>
</tr>
</tbody>
</table>
Planned post-authorisation development plan

**List of studies in post-authorisation development plan**

<table>
<thead>
<tr>
<th>Study/activity (including study number)</th>
<th>Objectives</th>
<th>Safety concerns /efficacy issue addressed</th>
<th>Status</th>
<th>Planned date for submission of (interim and) final results</th>
</tr>
</thead>
</table>
| PET image interpretation study (GE067-027) | **Primary Objective:** To assess the frequency of Vizamyl image reading errors in routine clinical practice in the EU  
**Secondary Objectives:** To assess the compliance of Vizamyl image readers with completion of the Vizamyl reader training programme  
To assess the understanding and compliance of doctors reading Vizamyl scans with the approved indication in the EU summary of product characteristics (SmPC) for Vizamyl  
To assess Vizamyl image reader performance on test images | Effectiveness of the Vizamyl reader-training programme in clinical practice by image readers (nuclear medicine physicians or radiologists with nuclear medicine training). | Ongoing | Start date: October 2018  
Recruitment end: 2022  
Final report: 2022 |
| Post-authorisation utilisation study (GE067-028) | **Primary Objective:** To determine the use of Vizamyl post-authorisation in the EU  
**Secondary Objectives:** To determine compliance with the Summary of Product Characteristics (SmPC) for Vizamyl  
To assess dosage and administration of Vizamyl  
To identify and characterise any use of Vizamyl in children  
To compare adverse event profiles of use of Vizamyl that is consistent with the SmPC and the use of Vizamyl that is inconsistent with the SmPC. | Off-label use | Ongoing | Start date: November 2019  
Recruitment end: 2022  
Final report: 2022 |

**Studies which are a condition of the marketing authorisation**

None.
Summary of changes to the risk management plan over time

Alignment with GVP: Module V – Risk management systems (Rev 2).

The following risks previously classified as important identified and important potential risks were reclassified and removed from the list of safety concerns:

- Allergic reactions
- Carcinogenicity and hereditary defects
- Lack of information on safety in patients with renal impairment
- Lack of information on safety in patients with hepatic impairment
- Lack of information about patients receiving more than one dose

Milestones for the ongoing and planned category 3 studies GE067-027 (assessing the effectiveness of the educational programme) and GE067-028 (characterising off-label use) have been updated.

This summary was last updated in 12/2019