VIZAMYL 150MBq/ml, solution for injection (flutemetamolum ^{18}F)

Summary of Risk Management Plan

Version 4 (based on RMP v2.3)

Date of report: April 2021

Marketing Authorisation Holder:

GE Healthcare AG, 8152 Opfikon, Switzerland

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/Information sur le médicament" 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/Information sur le médicament" (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.

Switzerland RMP Summary V 3 (Based on updated EU RMP, submitted December 2020)

Summary of the risk management plan (RMP) for Vizamyl (flutemetamol ^{18}F)

This is a summary of the risk management plan (RMP) for Vizamyl. The RMP details important risks of Vizamyl, how these risks can be minimised, and how more information will be obtained about Vizamyl's risks and uncertainties (missing information).

The reference document which is valid and relevant for the effective and safe use of Vizamyl in Switzerland is the "Arzneimittelinformation/Information sur le médicament"" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

This summary of the RMP for Vizamyl should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Vizamyl's RMP.

I. The medicine and what it is used for

Vizamyl is a radioactive diagnostic agent indicated for Positron Emission Tomography (PET) imaging of the brain to estimate β-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD) or other causes of cognitive decline. A negative Vizamyl scan indicates sparse to no neuritic plaques, and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to AD. A positive Vizamyl scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of neuritic plaque is present in patients with AD but may also be present in patients with other types of neurologic conditions, as well as older people with normal cognition. Vizamyl should always be used in conjunction with other clinical diagnostic evaluations.

Limitations of use:

- A positive Vizamyl scan alone does not establish a diagnosis of AD or other cognitive disorder
- Safety and effectiveness of Vizamyl have not been established for predicting the development of dementia or other neurological condition, or for monitoring responses to therapies

It contains flutemetamol (18F) as the active substance and it is given by intravenous route of administration.

Further information about the evaluation of Vizamyl's benefits can be found in Vizamyl's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage https://www.ema.europa.eu/en/medicines/human/EPAR/Vizamyl.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Vizamyl, together with measures to minimise such risks and the proposed studies for learning more about Vizamyl's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;
- The authorised pack size - the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status - the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Vizamyl, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of important risks and missing information

Important risks of Vizamyl are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Vizamyl. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information	
Important potential risks	PET imaging interpretation errors
	Off-label use

II.B Summary of important risks

Table 1 and Table 2 summarise the important risks associated with the use of Vizamyl.

Table 1 PET imaging interpretation errors

Important potential risk PET imaging interpretation errors	
Evidence for linking the risk to the medicine	The evidence is based on information from clinical studies.
Risk factors and risk groups	Unexperienced/untrained readers is a risk factor as they are more likely to experience image interpretation difficulties. Especially in patients with considerable brain atrophy there is a risk of image interpretation errors that could lead to an incorrect result of the investigation.[1]

[1] Revised text in the RMP Summary. The respective text in the EU RMP will be revised in due course. The approved EU Risk Management Plan version 2.3 states "Unexperienced/untrained readers is a risk factor as they are more likely to experience image interpretation difficulties. Patients with considerable brain atrophy that is not due to Alzheimer's disease, entails a risk of image interpretation error that could lead to a false positive result of the investigation".

Table 1 PET imaging interpretation errors

Important potential risk **PET imaging interpretation errors**	
Risk minimisation measures	Routine risk minimisation measures: – SmPC sections 4.2 and 4.4 which includes recommendations to have Vizamyl images interpreted by readers trained in the interpretation of PET images with flutemetamol (^{18}F), – Vizamyl is a prescription only medicine. Additional risk minimisation measure: – Educational programme.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: – GE067-027, Post-Authorisation Safety Study to Evaluate the Effectiveness of VIZAMYL™ Reader Training in Europe.

Table 2 Off-label use

Important potential risk **Off-label use**	
Evidence for linking the risk to the medicine	The evidence is based on scientific literature reports related to clinical trials with [^{11}C]PiB, a different amyloid imaging agent. These reports show that [^{11}C]PiB have been used for other purposes than diagnosis of Alzheimer's and in other population than those indicated for Vizamyl.
Risk factors and risk groups	Vizamyl could potentially be used for screening in patients not included by the indication, such as cognitively normal patients who are at risk for MCI or Alzheimer's disease.
Risk minimisation measures	Routine risk minimisation measures: – SmPC section 4.1 which includes the therapeutic indication for using Vizamyl – Vizamyl is a prescription only medicine Additional risk minimisation measure: – None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: – GE067-028, Post-Authorisation Survey of Nuclear Medicine Physicians and Radiologists in Europe to Evaluate Trends and Patterns in VIZAMYL™ Use in Everyday Clinical Practice in the EU.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of Vizamyl.

II.C.1 Other studies in post-authorisation development plan

Study short name: GE067-027

Purpose of the study: To assess compliance with completion of the educational programme, the effectiveness of the educational programme, the understanding and compliance of readers with the approved indication, and the frequency of reading errors in routine clinical practice.

Study short name: GE067-028

Purpose of the study: To determine the use of Vizamyl post-authorisation in the EU, including determining compliance with the Vizamyl SmPC, assessing dosage and administration of Vizamyl and comparing the adverse event profile between use of Vizamyl that is consistent with and inconsistent with the Vizamyl SmPC.

This summary was last updated in 04/2021