EMA/404996/2014

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

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. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Vizamyl, which can be found on Vizamyl's EPAR page.

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 ^{18}F. 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 doctors 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 risks

Risk	What is known	Preventability
Allergic reactions	Allergic reactions are uncommon and may affect up to 1 in 100 people. Symptoms of allergic reactions can include swelling of the face or eyes; pale, itchy or tight skin; rash; feeling short of breath; irritation of the throat or feeling sick. These symptoms may occur even when Vizamyl is used for the first time.	Vizamyl must not be used in patients who are allergic to flutemetamol ^{18}F or any other ingredients in Vizamyl.

Important potential risks

Risk	What is known
Inaccurate interpretation of Vizamyl PET scans	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 doctors reading Vizamyl scans has been implemented to minimise this risk.
Cancer or birth defects (carcinogenicity or hereditary defects)	Vizamyl delivers a very low amount of radiation which poses a minimal risk of cancer or any hereditary abnormalities. No cases of cancer or birth defects were observed in clinical studies. Pregnant women were excluded from the clinical studies with Vizamyl.
Lack of information on off-label use	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.

Missing information

Risk	What is known
Lack of information on safety in patients with reduced liver function (hepatic impairment)	A significant proportion of Vizamyl is removed from the body through the liver. Therefore in patients with reduced liver function an increased exposure to radiation is possible. From the limited clinical data available, the safety profile of Vizamyl use in patients with reduced liver function has not been characterised.

Risk	What is known
Lack of information on safety in patients with reduced kidney function (renal impairment)	Another significant proportion of Vizamyl is removed from the body through the kidneys. Therefore in patients with reduced kidney function an increased exposure to radiation is possible. From the limited clinical data available, the safety profile of Vizamyl use in patients with reduced kidney function has not been characterised.
Lack of information about patients receiving more than one dose	Vizamyl is unlikely to be given more than once or twice; if this occurs, the interval between scans is likely to be months or years, far longer than the time it takes to eliminate flutemetamol from the body; therefore, effects of repeat dosing are unlikely. However, information on patients receiving more than one dose and how this may affect patients' safety is limited.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) 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. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Vizamyl can be found on Vizamyl's EPAR page.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements of any educational material can be found in Annex II of the product information which is published on Vizamyl's EPAR page; how they are implemented in each country however will depend upon agreement between the marketing authorisation holder and the national authorities.

These additional risk minimisation measures are for the following risks:

Innacurate interpretation of Vizamyl PET scans

Risk minimisation measure: Healthcare professional educational programme
Objective and rationale: Doctors 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.
Description: Educational material and training to be provided to doctors who will be tested on reading Vizamyl PET scans. Some doctors will also be re-tested after 3 to 6 months as part of the post-authorisation PET image interpretation study GE067-027 (see table below).

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	**Objectives**	**Safety concerns / efficacy issue addressed**	**Status**	**Planned date for submission of (interim and) final results**
PET image interpretation study (GE067-027)	Primary Objective: To assess the frequency of Vizamyl image reading errors in routine clinical practice 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).	In planning	Approx. April 2018
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	Off-label use	In planning	Final Report: Approx. 4 years post-authorisation

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
	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.			

Studies which are a condition of the marketing authorisation

None.

Summary of changes to the risk management plan over time

Not applicable.

This summary was last updated in 07-2014.