Part VI Summary of the risk management plan

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Summary of safety concerns	
Important identified risks	• Hepatic disorders • Overdose/drug administration error with pump device
Important potential risks	• Prostate cancer
Missing information	• none

VI.1.2 Table of on-going and planned additional PhV studies/activities in the Pharmacovigilance Plan

Not applicable.

VI.1.3 Summary of Post authorisation efficacy development plan

No study planned.

VI.1.4 Summary table of risk minimisation measures

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Important identified risks		
Hepatic disorders	Included in SPC section • 4.8 Undesirable effects and in the PIL.	NA
Overdose/drug administration error with pump device	Information on the correct use of the pump device is included in SPC sections • 4.2 Posology and method of administration • 6.6 Special precautions for disposal and other handling and in the PIL.	NA
Important potential risks		
Prostate cancer	Currently available data do not support the need for risk minimisation measures.	NA
Missing information		
None	NA	NA

VI.2 Elements for a Public Summary

Memantine Stada 10mg/ml oral solution

VI.2.1 Overview of disease epidemiology

Alzheimer's disease (AD) is a brain disease that is characterised by reduction in cognitive function and memory (dementia). The disease continuously progresses and once started, cannot be cured. However, progression can be slowed down and symptoms can be controlled. Worldwide, approximately 24 million people are suffering from AD, and both genders are equally affected. The risk of developing AD increases dramatically with age. Whereas 53 new cases per 1 000 people are observed between the ages of 65 and 74 years, 231 new cases per 1 000 people occur in the age group of 85 years and older. Other risk factors that contribute to the likelihood of developing AD include a family history of the disease, genetic variation for a cholesterol-transporting protein (Apolipoprotein E-e4 (APOE-e4) gene), diagnosis of mild cognitive impairment, cardiovascular diseases, education (fewer years of education increases the risk), social and cognitive engagement and traumatic brain injury.

VI.2.2 Summary of treatment benefits

Memantine Stada belongs to a group of medicines known as anti-dementia medicines. Memory loss in Alzheimer's disease is due to a disturbance of message signals in the brain. The brain contains so-called N-methyl-D-aspartate (NMDA)-receptors that are involved in transmitting nerve signals important in learning and memory. Memantine Stada belongs to a group of medicines called NMDA-receptor antagonists. Memantine Stada acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

Memantine Stada is used for the treatment of patients with moderate to severe Alzheimer's disease, a progressive brain disorder that gradually affects memory, intellectual ability and behaviour.

A study in 252 outpatients suffering from moderate to severe Alzheimer's disease showed beneficial effects of memantine treatment in comparison to placebo after 6 months.

Another study of memantine in the treatment of mild to moderate Alzheimer's disease included 403 patients. Memantine-treated patients showed a statistically significant better effect than placebo-treated patients on their Alzheimer's disease assessment scale and CIBIC-plus scores at week 24.

A meta-analysis of patients with moderate to severe Alzheimer's disease from the six phase III, placebo-controlled, 6-month studies showed that memantine significantly improved cognitive, global, and functional capabilities. When patients were identified with concurrent worsening in all three domains, results showed a statistically significant effect of memantine in preventing worsening, as twice as many placebo-treated patients as memantine-treated patients showed worsening in all three domains.

VI.2.3 Unknowns relating to treatment benefits

Use in children younger than 18 years is not recommended due to lack of data on safety and efficacy; there is no relevant use of Memantine Stada in the paediatric population in the treatment of Alzheimer's disease.

Use in patients with severe hepatic impairment has not been studied, and treatment is therefore not recommended in this patient group.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Liver disorders (Hepatic disorders)	Elevated liver function tests have occurred in up to 1 in 10 patients treated with memantine. Liver inflammation (hepatitis) has also occurred during memantine therapy, but the frequency could not be estimated.	Symptoms that could be a sign of liver disorders include abdominal pain, yellowing of the white part of your eyes or your skin, malaise and dark urine. However, slight abnormalities in your liver enzyme levels will only be noticed on a blood test. If you experience any side effects that you think might be associated with a liver disorder, talk to your doctor or pharmacist for confirmation. They will advise you on the best course of action or order some additional tests. To minimise the risk of any side effects, always take the medicine as prescribed by your doctor and/or as indicated in the package leaflet.
Overdose/drug administration error with pump device	Several cases of memantine overdoses/medication errors associated with the pump device have been reported in the past. These resulted from confusion between the dosages delivered by a dropper and the pump.	Carefully read the dosing instructions in your package leaflet before administering the indicated dosage. Consult a healthcare professional if you are unsure about the proper administration of Memantine Stada.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Prostate cancer	Patients treated with the medicinal product may be at an increased risk of developing this safety concern.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.