EMA/707627/2015

Summary of the risk management plan (RMP) for Numient (levodopa / carbidopa)

This is a summary of the risk management plan (RMP) for Numient, which details the measures to be taken in order to ensure that Numient 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 Numient, which can be found on Numient's EPAR page.

Overview of disease epidemiology

Numient is used to treat the symptoms of Parkinson's disease, a progressive brain disorder that causes shaking and muscular stiffness and slows down movement.

Parkinson's disease gets worse slowly and it is the second most common cause of movement disorders due to nervous system disorders in the elderly. Severe disability or death may be expected in 25% of the patients within 5 years.

Parkinson's disease affects more than 6 million people worldwide, with an incidence of 10 to 26 cases per 100,000 person-years. Parkinson's disease is very rare in individuals under the age of 40 years, and symptoms generally appear in people between 55 and 65 years of age.

Other risk factors for Parkinson's disease include a family history, male gender, head injury, exposure to pesticides, consumption of well water and rural living.

Summary of treatment benefits

In a study of 381 patients with early stage Parkinson's disease, Numient at various doses was more effective at improving symptoms than placebo (a dummy treatment). After 30 weeks, patients taking Numient had their symptoms improve by an average of between 11.7 and 14.9 points (depending on dose) on a standard symptom scale (Unified Parkinson's Disease Rating Scale, UPDRS Part II and Part III). Patients who took placebo had an average improvement of 0.6 points.

A second study compared Numient with another treatment containing levodopa and carbidopa in 393 patients with advanced Parkinson's disease. This study looked at how well the treatments reduced the time when patients have more difficulty moving about, called 'off periods'. After 13 weeks, patients taking Numient had off periods of about 24% of their waking hours compared with 30% of waking hours in patients taking the comparator medicine. Both groups had off periods of about 36-37% at the start of the study.

Unknowns relating to treatment benefits

Because of the extensive clinical experience with other treatment combining levodopa and carbidopa, no difference in terms of benefits is expected in the different sub-populations.

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Involuntary muscle movements (also called dyskinesias)	Medicines containing levodopa cause dyskinesias. Carbidopa decreases the breakdown of levodopa in the blood and improves delivery of levodopa to the brain. Higher levels of levodopa in the brain can cause dyskinesias.	Patients should be monitored for dyskinesia. If dyskinesias occur, dose reduction should be considered.
Psychiatric events	Medicines containing levodopa can cause mental disturbances such as hallucinations.	Numient should be used with caution in patients with past or current psychotic disorders.
Impulse control disorders	Medicines containing levodopa can reduce control over impulsive behaviour and result in effects such as pathological gambling, increased libido, hypersexuality, compulsive spending or buying, and compulsive eating.	Patients should be regularly monitored for the development of impulse control disorders. Patients and caregivers should be made aware of the symptoms of impulse control disorders. Doctors should review the patient's treatment with Numient if such symptoms develop.
Postural hypotension, i.e a sudden fall of blood pressure on standing or sitting up	Products containing levodopa are associated with postural hypotension episodes. This risk is common (it occurs in up to 1 patient in 10).	Numient should be used with caution in patients also taking medicines for high blood pressure.
Sudden onset of sleep/ somnolence	Products containing levodopa are associated with somnolence and episodes of sudden sleep onset.	Patients who feel unusually sleepy or have had an episode of sudden sleep onset must not drive or operate machines. The doctor may also consider reducing the dose or stopping treatment with Numient.
Neuroleptic malignant syndrome (NMS), i.e. a life-threatening neurologic emergency	Cases resembling NMS have been reported with medicines containing levodopa/carbidopa when the dose was stopped or abruptly reduced.	Patients should be observed carefully when the dose is reduced abruptly or discontinued, especially if the patient is receiving antipsychotics.

Important potential risks

Risk	What is known
Melanoma, a type of skin cancer	Patients with Parkinson's are at increased risk of melanoma but it is not clear whether the increased risk is due to the disease or the treatment.

Missing information

None.

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 Numient can be found on Numient's EPAR page.

This medicine has no additional risk minimisation measures.

Planned post-authorisation development plan

There are no planned post-authorisation studies.

Studies which are a condition of the marketing authorisation

Not applicable

Summary of changes to the risk management plan over time

Not applicable.

This summary was last updated in 10-2015.