PUBLIC SUMMARY OF RISK MANAGEMENT PLAN (RMP)

ENTACAPONE ORION PHARMA 200 MG TABLET

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VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Parkinson's disease (PD) is a progressive brain disease affecting mainly elderly people. The classical motor symptoms of PD are slowness of movements, muscle stiffness and tremor at rest. Also balance problems are relatively common in later disease. Although not usually present at the time of diagnosis, some patients will develop for example cognitive problems, excessive daytime sleepiness and hallucinations after many years into the disease. Also constipation, urinary incontinense, drop in blood pressure upon standing with subsequent dizziness and various pains may be related to PD.

The occurrence of PD is increasing with increasing age and PD is rare before age of 50 years. 0.3% of the entire population and 1% of people over 60 years of age have PD. It is estimated that approximately 10-20 out of a population of 100 000 people will develop PD in every year. There are no significant differences in the occurrence of PD between men and women or between different races. In general, geographical differences are not known either and PD is equally common in different European countries.

Long and excessive exposure to herbicides, pesticides and heavy metals may increase the risk of PD. On the other hand, smoking and coffee are known to decrease the risk of PD. Genetic mutations causing PD are relatively rare.

VI.2.2 Summary of treatment benefits

The main cause of Parkinson's disease is low levels of dopamine in the brain. Drug treatments for Parkinson's disease aim to increase the levels of dopamine. Levodopa is a dopamine precursor which is always given together with another drug (carbidopa or benserazide) to decrease the breakdown of levodopa before it enters into the brain. The long-term problems associated with levodopa are so called response fluctuations (also called as wearing-off) when the response to levodopa varies during the day between "ON" (time when there is a satisfactory response to levodopa with relatively minor parkinsonian symptoms) and "OFF" (time when the good response has disappeared and parkinsonian symptoms are negatively affecting normal daily activities).

Entacapone is a drug, which also decreases the breakdown of levodopa, but with another mechanism than carbidopa and benserazide. Therefore, entacapone prolongs the beneficial response to levodopa and can therefore be added to levodopa treatment in order to further decrease response fluctuations. In two studies with a total of 376 patients with Parkinson's disease and response fluctuations (171 patients in study I and 205 patients in study II), entacapone or placebo was given with each levodopa dose. In these studies, entacapone decreased response fluctuations (measured by duration of OFF-time) more than placebo. The decrease in OFF-time was 24 % in the entacapone group and 0 % in the placebo group in study I. The corresponding figures in study II were 18 % and 5 %.

VI.2.3 Unknowns relating to treatment benefits

Controlled clinical studies and clinical practice have shown that the efficacy of entacapone is similar in adults of different ages and between men and women and different races.

There is no or very limited experience of levodopa/carbidopa/entacapone during pregnancy or in children.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Neuroleptic malignant syndrome A rare severe reaction to medicines used to treat disorders of the central nervous system, which typically consists of high fever, muscle rigidity, tremor, agitation, confusion, rapid pulse and/or wide fluctuations in blood pressure as well as changes in specific muscular enzyme in the blood stream (creatine phosphokinase).	Isolated cases of neuroleptic malignant syndrome have been reported. This may occur especially when entacapone and other medicines to treat Parkinson's disease are suddenly stopped or the dose is suddenly reduced.	Discontinuation of the treatment with entacapone and other Parkinson's medicines should proceed slowly. Entacapone should not be used if patient has previously experienced neuroleptic malignant syndrome.
Rhabdomyolysis A condition, which typically consists of muscular pain and may be associated with fever, confusion and decreased consciousness. This condition causes skeletal muscle tissue damage and break down, which is associated with release of muscular break down products (such as muscular protein called myoglobin) into the blood stream. These break down products may be especially harmful for kidneys and lead to impaired function of the kidneys.	Rhabdomyolysis is mainly associated with severe dyskinesias or neuroleptic malignant syndrome and it has been observed rarely in patients with Parkinson's disease.	Discontinuation of the treatment with entacapone and other Parkinson's medicines should proceed slowly. Entacapone should not be used if patient has previously experienced rhabbdomyolysis which was not caused by injury.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Myocardial infarction and other ischaemic heart disease Events caused by lack of oxygen in the heart.	Slight increase in myocardial infarction and other ischemic heart disease events was seen in clinical studies done with entacapone. However, in a recent epidemiological study published in the scientific journal, entacapone treatment was not reported to be associated with an increased risk of acute myocardial infarction, stroke, or death in elderly patients with Parkinson's disease.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) 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. The Summary of Product Characteristics and the Package leaflet for this medicinal product can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable.