2. Elements for a public summary

2.1 Overview of disease epidemiology

PD is a progressive neurodegenerative disorder that is characterized by the symptoms of resting shiverslow movements, stiffness, and postural instability. After Alzheimer's disease, it is the second most common neurodegenerative disease, affecting approximately 1-2% of the European population over the age of 65 years. The incidence of PD increases with age. (Hoy and Keating 2012; Oldfield et al. 2007)

2.2 Summary of treatment benefits

Restoration of the dopaminergic coverage forms the central strategy for the treatment of PD. Thus, levodopa forms the backbone of therapy of PD. Other antiparkinsonian substances, such as dopamine agonists and MAO-B inhibitors are used as monotherapy or in addition to levodopa in patients with moderate to advanced disease. (Martindale 2014; Oldfield et al. 2007)

MAO-B is the major enzyme responsible for the degradation of dopamine in the human brain. Therefore, selective MAO-B inhibitors, such as rasagiline are an important therapeutic option for patients with PD. (Hoy and Keating 2012; Oldfield et al. 2007)

2.3 Unknowns relating to treatment benefits

The safety and efficacy of rasagiline in children and adolescents have not been established. No data are available.

2.4 Summary of Safety Concerns

Important identified risks

Risk	**What is known**	**Preventability**
Decreased blood pressure when used together with levodopa	Decrease in blood pressure when rising to a standing position, with symptoms such as dizziness/light-headedness may occur by concomitant use with levodopa.	Patients should be informed and monitored. They should tell their physician if symptoms occur.
Obsessive thoughts or impulsive behavior (impulse control disorders)	There have been cases of patients who, while taking medications for the treatment of Parkinson's disease, were unable to resist the impulse, urges or cravings to carry out harmful activities to themselves or others.	Patients or caregivers should tell the doctor if the patient develops unusual behavior or were unable to resist the impulse to perform potentially harmful actions.
Severe side effects with with other antidepressive drugs (serotonin syndrome)	Severe side effects such as excitement, confusion, increased body temperature, have been observed	Patients should be monitored carefully
Concomitant use of drugs used for the treatment of depression (selective	Serious adverse effects have been observed with concomitant use of	Concomitant use with other antidepressants or CYP1A2 inhibitors should

serotonin reuptake inhibitors (SSRI), selective noradrenaline reuptake inhibitors (SNRI), or tricyclic or tetracyclic antidepressants), inhibitors of CYP1A2, (enzyme for the degradation of rasagiline) or other drugs which are used for the treatment of depression or Parkinson's disease (inhibitors of MAO)	rasagiline and SSRIs, SNRIs, or tricyclic/tetracyclic antidepressants. Combination of rasagiline with other MAO inhibitors may lead to a critical increase in blood pressure.	be done with caution. Rasagiline should not be used together with other MAO inhibitors. There should be at least 14 days between stopping rasagiline and starting a MAO inhibitor.

Important potential risks

Risk	**What is known**
Risk of melanoma	Skin cancer has been reported in around 1% of patients in controlled clinical trials. The data collected from trials indicate that Parkinson's disease and not any medicine in particular is associated with a higher risk of melanoma.
Elevated blood pressure	A few cases of elevated blood pressure have been reported during marketing of the drug
Concomitant use of a potent pain killer (pethidine) or substances present in eye or nasal drops or cold medicines (sympathomimetics)	Combination of rasagiline with a potent pain killer pethidine may result in serious adverse effects. Interactions (increased MAO activity) have been observed between rasagiline and sympathomimetics.

Missing information

Risk	**What is known**
Use during pregnancy and breast-feeding	There is no information on safety and efficacy of rasagiline in pregnant or breast-feeding women. Therefore, rasagiline should not be used during pregnancy and breast-feeding.

2.5 Summary of additional risk minimisation measures by safety concern

No additional risk minimization measures are planned.

2.6 Planned post-authorisation development plan

NA

2.7 Summary of changes to the risk management plan over time

NA