VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Parkinson's disease is the most common neurodegenerative disorder after Alzheimer's disease. It is estimated that 6.3 million people worldwide suffer from Parkinson's disease, of which 1.2 million are in Europe. The disease affects all races and the age of onset is usually over 60 years, although one in ten sufferers are diagnosed before the age of 50 years. The incidence is predicted to double by 2050, as a result of an ageing population. Parkinson's disease is slightly more prevalent in men than women (1).

VI.2.2 Summary of treatment benefits

Ropinirole is used to treat Parkinson's disease, a condition in which patients have low levels of a hormone called dopamine in the brain, resulting in gradually worsening movement disorders. Ropinirole has effects similar to those of natural dopamine, so it helps to reduce the symptoms of Parkinson's disease.

A 24-week study demonstrated that ropinirole prolonged-release tablets were more effective in treating Parkinson's disease in patients whose symptoms were not controlled by levodopa compared to placebo. A 36-week study showed that prolonged-release tablets were as effective as immediate release tablets in treating the disease.

These studies were conducted for Requip – Modutab Retardtabletten by GlaxoSmithKline and not by Mylan.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Table 1 Part VI - Summary table of safety concerns

Important identified risks

Risk	What is known	Preventability
Hallucinations	A profound distortion in a person's perception of reality, typically accompanied by a powerful sense of reality. A hallucination may be a sensory experience in which a person can see, hear, smell, taste, or feel something that is not there.	Patients should tell their doctor if they, or their family or carer, notice that they are suffering from symptoms of hallucination. Dose reduction or gradual discontinuation should be considered if such symptoms develop.

Risk	What is known	Preventability
Hypotension/orthostatic hypotension	Hypotension/orthostatic hypotension occur due to lowering of blood pressure. Symptoms can include light-headedness, weakness, blurred vision and syncope or passing out.	Patients should tell their doctor if they, or their family or carer, notice that they are developing are suffering symptoms of hypotension/orthostatic hypotension, furthermore, if patients present with such symptoms with ropinirole use they should be recommended to stop driving and if working or operating with heavy machinery, this should be discontinued until the matter has resolved to avoid any injury. Dose reduction or gradual discontinuation should be

Risk	What is known	Preventability
		considered if such symptoms develop.

Risk	What is known	Preventability
Syncope	Syncope is defined as a transient, self-limited loss of consciousness with an inability to maintain postural tone that is followed by spontaneous recovery. This definition excludes seizures, coma, shock, or other states of altered consciousness.	Patients should tell their doctor if they, or their family or carer, if they present with episodes of syncope. Dose reduction or gradual discontinuation should be considered if such symptoms develop.

Risk	What is known	Preventability
Sudden onset of sleep and excessive daytime somnolescence	People suffer from day time sleepiness, drowsiness and potential onset of sudden sleep. Product is POM.	Patients should tell their doctor if they, or their family or carer, if patients present with such symptoms with ropinirole use they should be recommended to stop driving and if working or operating with heavy machinery, this should be discontinued until the matter has resolved to avoid any injury. Dose reduction or gradual

Risk	What is known	Preventability
		discontinuation should be considered if such symptoms develop.

Risk	What is known	Preventability
Failure to resist urges, temptations or impulses that may harm oneself or others (Impulse control disorders)	The inability to resist the impulse, drive or temptation to perform an action that could be harmful to the patient or others may occur whilst using ropinirole. Such behaviours include strong impulses to gamble excessively, altered or increased sexual interest and behaviour, excessive eating and uncontrollable excessive shopping and spending.	Patients should tell their doctor if they, or their family or carer, notice that they are developing urges or cravings to behave in ways that are unusual for them and they cannot resist the impulse, drive or temptation to carry out certain activities that could harm themselves or others. Dose reduction or gradual discontinuation should be considered if such symptoms develop.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Fibrotic Complications	Reports of fibrotic complications such as retroperitoneal fibrosis, pulmonary infiltrates and pericarditis have been found in patients receiving treatment with ergot derived dopaminergic agents such as pergolide, drug discontinuation may resolve such complications however complete recovery

Risk	What is known (Including reason why it is considered a potential risk)
	does not always occur. It is unknown whether other dopamine agonists which do have an ergot structure such as ropinirole can cause such complications. Some cases of pleural fibrosis and insterstitial lung disease has been reported in postmarketing experience for ropinirole. While the evidence is not sufficient to establish a causal relationship between ropinirole and these fibrotic complications, a contribution of ropinirole cannot be excluded. Health Care Professionals should keep close observations on patients if such complications occur.

Risk	What is known (Including reason why it is considered a potential risk)
Cardiac rhythm disorders or effect on cardiac repolarisation.	As per clinical studies, changes in the QT interval and QT prolongation has been observed with doses of 4mg/day of ropinirole, however the effect of ropinirole at higher doses has not been systemically evaluated. Therefore, changes in QT interval and prolongation cannot be excluded.

Risk	What is known (Including reason why it is considered a potential risk)
Melanoma	Studies have shown that patients suffering from Parkinsons Disease have a higher risk of developing melanoma in comparison to the general population. It is not know whether the increased risk is due to Parkinsons Disease or due to other factors such as drugs use to treat the illness. Therefore, it is important that patients and health care professionals keep close observations to see whether the patient develops melanoma, periodic skin examinations are recommended.

Risk	What is known (Including reason why it is considered a potential risk)
Medication Errors	At high doses Ropinirole can increase the level of dopaminergic activity. In studies, patients who received a dose greater than 24mg/day reported symptoms of visual hallucinations, hyperhidrosis, claustrophobia, chorea and palpitations. Therefore caution should be taken when prescribing the medication and patients should be warned.

Risk	What is known (Including reason why it is considered a potential risk)
Haematopoiesis disorders	Haematopoiesisis the process of formation of blood or blood cells in the living body. Disorders of blood forming capacity can be detrimental. Therefore, it is important that patients and health care professionals keep close observations to see whether the patient develops any form of blood forming disorders and caution should be taken when prescribing the medication and patients should be warned.

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. 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 studies planned.

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

Not applicable.