VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Parkinson's disease (PD) is a neurodegenerative disorder characterized by bradykinesia, rigidity, postural imbalance and tremor. The incidence of PD increases with age and on average, 2 to 3% of the population in the western world will develop PD. The cause of the disease is still unknown.

VI.2.2 Summary of treatment benefits

Pramipexole is a dopamine agonist that binds with high selectivity and specificity to the D2 subfamily of dopamine receptors of which it has a preferential affinity to D3 receptors, and has full intrinsic activity.

In patients pramipexole alleviates signs and symptoms of idiopathic Parkinson' s disease. Controlled clinical trials included approximately 2100 patients of Hoehn and Yahr stages I – IV. Out of these, approximately 900 were in more advanced stages, received concomitant levodopa therapy, and suffered from motor complications. In early and advanced Parkinson's disease, efficacy of pramipexole in the controlled clinical trials was maintained for approximately six months. In open continuation trials lasting for more than three years there were no signs of decreasing efficacy. In a controlled double blind clinical trial of 2 year duration, initial treatment with pramipexole significantly delayed the onset of motor complications, and reduced their occurrence compared to initial treatment with levodopa. This delay in motor complications with pramipexole should be balanced against a greater improvement in motor function with levodopa (as measured by the mean change in UPDRS-score). The overall incidence of hallucinations and somnolence was generally higher in the escalation phase with the pramipexole group. However there was no significant difference during the maintenance phase. These points should be considered when initiating pramipexole treatment in patients with Parkinson´s disease.

VI.2.3 Unknowns relating to treatment benefits

Not applicable

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Excessive eating or spending, addictive gambling, an abnormally high sex drive or preoccupation with an increase in sexual thoughts or feelings (binge eating, compulsive shopping, pathological gambling, hypersexuality) and other abnormal behaviour	You may experience the following side effects: - Strong impulse to gamble excessively despite serious personal or family consequences. - Binge eating (eating large amounts of food in a short time period) or compulsive	Tell your doctor if you have (had) or develop any such conditions or symptoms.

Risk	What is known	Preventability
	eating (eating more food than normal and more than is needed to satisfy your hunger) - Uncontrollable excessive shopping or spending - Altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive.	
Inappropriate antidiuretic hormone secretion	Inappropriate antidiuretic hormone secretion can be an uncommon side effect (may affect up to 1 in 100 people).	Not known
Heart problems which can cause shortness of breath or ankle swelling (cardiac failure)	Heart problems can be an uncommon side effect (may affect up to 1 in 100 people).	Not known
Seeing, hearing or feeling things that are not there (Hallucinations) and confusion	Hallucinations and confusion can be a common side effect (may affect up to 1 in 10 people).	Tell your doctor if you have (had) or develop any such conditions or symptoms. If affected, do not drive or use machines.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Suicide-related behaviour	Tell your doctor if you or your family/carer notices that you are developing an impulse, drive or temptation to carry out certain activities that could harm yourself.
Augmentation, post treatment worsening after withdrawal and rebound in patients with restless legs syndrome	Another pharmaceutical form (immediate release tablets) of pramipexole can be used to treat patients with a different disease (restless legs syndrome). However, this risk is not applicable for patients with Parkinson's disease that are treated with Pramipexole prolonged-release tablets.
Delirium/mania	Tell your doctor if you or your family/carer notices that you are developing mania (agitation, feeling elated or over-excited) or delirium (decreased awareness, confusion, loss of reality). Your doctor may need to adjust or stop your dose.
Eye disorder (retinal degeneration)	Retinal degeneration was seen in rats receiving pramipexole but not in in any other animal species investigated or in man. You should have regular eye examinations during treatment with pramipexole.

Risk	What is known (Including reason why it is considered a potential risk)
Skin cancer (skin melanoma)	People who have Parkinson's disease may have a greater risk of developing melanoma (a type of skin cancer) than people who do not have Parkinson's disease. There is not enough information to tell whether medications used to treat Parkinson's disease such as pramipexole increase the risk of developing skin cancer.
Scar tissue (fibrotic events)	An increased risk of fibrotic events has been associated with other medicinal products used for therapy of Parkinson's disease. The relevance of this finding for pramipexole is not known.
Response-based behaviour	Not known.

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. This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post authorization studies have been planned. Only routine Pharmacovigilance activities will be performed to monitor the safety profile of the product, assuring a continuous assessment of safety of the product.

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

Table 1. Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0 and 2.0	Not applicable	Not applicable	Internal Versions
3.0	25-Nov-2013	• Not applicable	Preapproval Version
3.1	30-May-2014	**Identified Risks** • Binge eating, compulsive shopping, pathological gambling, hypersexuality and other abnormal behaviour. • Inappropriate antidiuretic hormone secretion • Cardiac failure • Hallucinations and confusion **Potential Risks** • Suicide-related behaviour • Augmentation, post treatment worsening after withdrawal and rebound in patients with restless legs syndrome (applicable for Immediate Release Tablets only)	

Version	Date	Safety Concerns	Comment
		• Delirium/mania • Skin melanoma • Fibrotic events • Response-based behaviour **Missing information** None	