VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Erectile dysfunction

Male erectile dysfunction (sometimes called impotence), is the inability to get, or keep, a hard penis (erection) sufficient for satisfactory sexual activity. Erectile dysfunction affects 50% of men older than 40 years, exerting substantial effects on quality of life. This common problem is complex and involves multiple pathways. Penile erections are produced by an integration of physiologic processes involving the central nervous, peripheral nervous, hormonal, and vascular systems. Any abnormality in these systems, whether from medication or disease, has a significant impact on the ability to develop and sustain an erection, ejaculate, and experience orgasm.

Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is when the prostate gland gets bigger with age. Symptoms include difficulty in starting to pass water, a feeling of not completely emptying the bladder and a more frequent need to pass water even at night.

BPH is a common problem that affects the quality of life in approximately one third of men older than 50 years. Worldwide, approximately 30 million men have symptoms related to BPH.

VI.2.2 Summary of treatment benefits

Erectile dysfunction

Tadalafil was significantly more effective than placebo in all studies in erectile dysfunction. For one of the questionnaires, where the maximum score is 30, patients who recorded scores of about 15 before treatment, recorded scores of 22.6 or 25 after receiving tadalafil 10 mg or 20 mg, respectively. Overall, in the studies of general populations, 81% of patients reported that tadalafil 'on demand' improved their erections as compared to 35% of those taking placebo. Patients taking tadalafil once a day at doses of 2.5 or 5 mg also reported improved erections compared with those taking placebo.

Benign prostatic hyperplasia

Tadalafil given at a dose of 5 mg was also more effective than placebo in all the studies in patients with benign prostatic hyperplasia, with the results showing a significant improvement in symptoms compared with placebo.

VI.2.3 Unknowns relating to treatment benefits

Data show that more patients aged 75 years and older had more tadalafil related adverse events compared to patients below 75 years of age. Although in general there were no important differences diarrhoea and dizziness were more frequent in older patients. Acknowledging that the size of the sample is low, given that these patients constitute a relevant target population the need to generate more data in this population has been added as missing information in the RMP.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Prolonged and possibly painful erection (priapism)	Prolonged and possibly painful erection after taking tadalafil has been reported rarely. Tadalafil should be used with caution in patients with anatomical deformation of the penis or in patients who have conditions which may predispose them to prolonged and possibly painful erections.	Before taking the tablets, tell your doctor if you have: - sickle cell anaemia (an abnormality of red blood cells). - multiple myeloma (cancer of the bone marrow). - leukaemia (cancer of the blood cells). - any deformation of your penis. If you experience prolonged and possibly painful erection after taking tadalafil which lasts continuously for more than 4 hours you should stop using the medicine and contact a doctor immediately.
Blood pressure decreased	Tadalafil should not be used in patients that have low blood pressure, uncontrolled high blood pressure, and patients taking group of medicines ("nitrates") used in the treatment of	Do not take tadalafil: - if you are taking any form of organic nitrate or nitric oxide donors such as amyl nitrite. If you are taking any form of nitrate or are unsure tell your

Risk	What is known	Preventability
	angina pectoris (“chest pain”). Caution is advised when taking tadalafil together with alpha blockers (drugs used to treat high blood pressure or urinary symptoms associated with benign prostatic hyperplasia) and other medicines to treat high blood pressure. Low blood pressure is an uncommon possible side effect of tadalafil.	doctor. - if you have low blood pressure or uncontrolled high blood pressure. Drinking alcohol may temporarily lower your blood pressure. If you have taken or are planning to take tadalafil avoid excessive drinking (blood alcohol level of 0.08 % or greater), since this may increase the risk of dizziness when standing up.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Stroke of the eye (nonarteritic anterior ischemic optic neuropathy (NAION))	Tadalafil should not be used in patients that ever had loss of vision because of non-arteritic anterior ischemic optic neuropathy (NAION), a condition described as “stroke of the eye”. If sudden decrease or loss of vision is noted, tadalafil should be stopped and the doctor contacted immediately.
Sudden hearing loss	Sudden decrease or loss of hearing has been reported as a rare possible side effect of tadalafil.

Missing information

Risk	What is known
Characterization of adverse events in elderly patients (≥65 years)	In the currently small sample size data show that more patients aged 75 years and older had more tadalafil related adverse event compared to patients below 75 years of age. Although in general there were no important differences diarrhoea and dizziness were more frequent in older patients.

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

Not applicable.

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

Table 2. Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	6 December 2012	Identified Risks: •Priapism •Hypotension/increased hypotensive effect Potential Risks: • Nonarteritic anterior ischemic optic neuropathy (NAION) • Sudden hearing loss Missing information: • Characterization of adverse events in elderly patients (≥65 years)	Safety concerns adopted as per available data from originator's RMP