PART VI: SUMMARY OF ACTIVITIES IN THE RISK MANAGEMENT PLAN BY PRODUCT

VI1. Elements for summary tables in the EPAR

VI1.1. Summary Table of Safety Concerns

Summary of Safety Concerns	
Important identified risks	– Priapism – Hypotension/increased hypotensive effect
Important potential risks	– Non-arteritic anterior ischemic optic neuropathy (NAION) – Sudden hearing loss
Missing information	– Characterisation of adverse events in elderly patients (≥65 years)

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

None

VI.1.3 Summary of Post authorisation efficacy development plan

Not applicable

VI1.4. Summary Table of Risk Minimisation Measures

Safety Concern	**Routine Risk Minimisation Measures**	**Additional Risk Minimisation Measures**
Important identified risks		
Priapism	Text in SmPC section 4.4 Special warnings and precautions for use and 4.8 Undesirable effects	None
Hypotension/increased hypotensive effect	Text in SmPC section 4.3 Contraindications, 4.4 Special warnings and precautions for use, 4.5 Interaction with other medicinal products and other forms of interaction and 4.8 Undesirable effects	None
Important potential risks		

Non-arteritic anterior ischemic optic neuropathy (NAION)	Text in SmPC Section 4.3 Contraindications , 4.4 Special warnings and precautions for use and 4.8 Undesirable effects	None
Sudden hearing loss	Text in SmPC Section 4.8 Undesirable effects	None
Missing information		
Characterisation of adverse events in elderly patients (≥65 years)	Text in SmPC Section 4.8 Undesirable effects and 5.2 Pharmacokinetic properties	None

VI2. Elements for a public summary

VI2.1. Overview of Disease Epidemiology

Erectile dysfunction (ED) is the inability to attain and maintain an erection sufficient for satisfactory sexual performance. Although a benign disorder, it can have a significant impact on the quality of life of sufferers, partners and families. It is important also to consider the physical and psychosocial health of the sufferer. Patients should be properly assessed and investigated before embarking on treatment. The incidence and prevalence is high worldwide. The first large-scale community study - the Massachusetts Male Ageing Study - showed that 52% of men (aged 40 to 70 years) were affected at some time (mild 17%; moderate 25%; severe 10%). A Cologne study reported that ED was the most prevalent of the male sexual dysfunctions (prevalence age 30 to 80 years) at 19.2% as compared to 31% for all types of male sexual dysfunction. This study equates to about 26 new cases annually per 1,000 men. Whichever study, country or methodology is used, this is clearly a significant condition likely to present regularly to a GP on average between 1 and 4 times per month. Significant media interest has led more men to seek help for ED. There is in all studies a steep age-related increase. The Cologne study found that of men aged 30-80 years, the prevalence rose from 2.3% at age 30 to 53.4% at age 80. Only about 10-20% of patients with erectile dysfunction are believed to have a solely psychogenic cause but psychogenic factors are often present in those who are diagnosed as having a physical cause.[1,2]

VI2.2. Summary of Treatment Benefits

Tadalafil Aurovitas, Tadalafil Glob, Tadalafil Arrow or Tadalafil is indicated for the following

- Treatment of erectile dysfunction in adult males.

[1] Guidelines on Male Sexual Dysfunction: Erectile dysfunction and premature ejaculation, European Association of Urology (2013)

2 San Martin C, Simonelli C, Sonksen J, et al; Perceptions and opinions of men and women on a man's sexual confidence and its relationship to ED: results of the European Sexual Confidence Survey. Int J Impot Res. 2012 Nov-Dec; 24(6):234-41. doi: 10.1038/ijir.2012.23. Epub 2012 Jun 21

- In order for tadalafil to be effective, sexual stimulation is required.

Tadalafil is not indicated for use by women

VI2.3. Unknowns Relating to Treatment Benefits

There are no unknowns relating to treatment benefits that the MAH is aware of.

VI2.4. Summary of Safety Concerns

Important Identified Risks

Risk	What is Known	Preventability
Priapism	Patients who experience erections lasting 4 hours or more should be instructed to seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency may result. Tadalafil should be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease), or in patients who have conditions which may predispose them to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia).	Patient should inform their doctor if they have any blood disorders, cancer of the bone marrow or cancer of the blood cells. The product should be used with caution by these patients. Physician supervision and care.
Hypotension/increased hypotensive effect	In clinical studies, tadalafil was shown to augment the hypotensive effects of nitrates. This is thought to result from the combined effects of nitrates and tadalafil on the nitric oxide/cGMP pathway. Therefore, administration of tadalafil to patients who are using any form of organic nitrate is contraindicated In patients who are taking alpha1 blockers, concomitant administration of tadalafil may lead to symptomatic hypotension in some patients. The combination of tadalafil and doxazosin is not recommended.	Patients should inform their doctor if they are taking any form of nitrate medicines, as tadalafil should not be used by patients who are on these medications. Patients should also inform their doctor or pharmacist if they are taking any medications used to treat high blood pressure. A possible dose adjustment of these medicines may be required. Physician supervision and care.

Important potential risks

Risk	What is Known	Preventability
Non-arteritic anterior ischemic optic neuropathy (NAION)	Tadalafil is contraindicated in patients who have loss of vision in one eye because of	Drug should be discontinued imeediately

	non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure. Visual defects and cases of NAION have been reported in connection with the intake of tadalafil and other PDE5 inhibitors. The patient should be advised that in case of sudden visual defect, he should stop taking Tadalafil and consult a physician immediately	Patients should not take tadalafil if they have ever experienced loss of vision in one eye, regardless of whether this was experienced whilst taking tadalafil or medicines of the same family, or not. Physician supervision and care.
Sudden hearing loss	In rare cases, the use of tadalafil may lead to sudden hearing loss.	Drug should be discontinued immediately Patients should contact their doctor immediately if they experience sudden decrease or loss of hearing while taking tadalafil.

Missing information

Risk	What is known
Characterisation of adverse events in elderly patients (≥65 years)	Data in patients over 65 years of age receiving tadalafil in clinical trials, either for the treatment of erectile dysfunction or the treatment of benign prostatic hyperplasia, are limited. In clinical trials with tadalafil 5mg taken once a day for the treatment of benign prostatic hyperplasia, dizziness and diarrhoea were reported more frequently in patients over 75 years of age Healthy elderly subjects (65 years or over), had a lower oral clearance of tadalafil, resulting in 25 % higher exposure (AUC) relative to healthy subjects aged 19 to 45 years. This effect of age is not clinically significant and does not warrant a dose adjustment

VI2.5. Summary of Additional Risk Minimisation Measures by Safety Concern

Not applicable.

VI2.6. Planned Post Authorisation Development Plan

Not applicable.

Studies Which are a Condition of the Marketing Authorisation

None.

VI2.7. Summary of Changes to the Risk Management Plan over time

Major Changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
NA	NA	NA	NA