VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Erectile dysfunction

Erectile dysfunction (ED) or impotence is sexual dysfunction characterized by the inability to attain or maintain an erection of the penis for satisfactory sexual performance. This can occur at any age, but is more common in men over age 75 and in middle aged men, ED can signal risk of a heart attack. Conditions affecting the flow of blood and physical structure of penis, nervous system and hormone levels can cause an ED. In a European study, men aged 30–80 years, the occurence of self-reported ED was 19.2 per 100 individuals, with a age-related increase from 2.3 per 100 individuals to 53.4 per 100 individuals. The worldwide population of ED is very high and is expected to increase substantially over the next 25 years. Treatment included psychotherapy, oral medications and surgeries.

VI.2.2 Summary of treatment benefits

The efficacy of Vardenafil compared with placebo in 17,000 men with erectile dysfunction (ED) aged 18-89 years, many of whom were already suffered from other disease. A post-prostatectomy patients (in this patient, surgery was already done for removal of all or part of the prostate gland) and diabetes mellitus patients(patient with a high blood sugar levels), who received 10 mg and 20 mg vardenafil and in a spinal cord injured patient who received flexible-dose of vardenafil has significantly improved the erectile function domain score, the ability to obtain and maintain an erection long enough for successful intercourse and penile rigidity compared to placebo.

People treated with vardenafil resulted in an improvement of erectile function compared to placebo. In the small number of patients who attempted intercourse up to four to five hours after dosing the success rate for penetration and maintenance of erection was consistently greater than placebo.

VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy data are established in the targeted population.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Allergic reaction (Hypersensitivity)	Vardenafil rarely cause an allergic reaction in 1 out of 1,000 people. Signs of an allergic reaction include a rash, itching, swollen face or lips and shortness of breath.	Do not take vardenafil if patients are allergic to vardenafil or any of the other ingredients of this medicine.
Decrease in blood pressure (Hypotension)	Vardenafil rarely cause low blood pressure in 1 out of 1,000 people.	Do not take vardenafil if patients have or have had low blood pressure. Do not take medicines containing nitrates, such as glycerol trinitrate for chest pain, or nitric oxide donors, such as amyl nitrite. Taking these medicines with vardenafil could seriously affect your blood pressure.
Abnormal electrical conduction within	Single oral doses of 10 mg and 80 mg of vardenafil have been	If a patient experience abnormal electrical conduction

Risk	What is known	Preventability
the heart (Effects on QT-interval and cardiac rhythm) (arrhythmias)	shown to prolong electrical conduction within the heart Medicinal products that may prolong electrical conduction within the heart, including vardenafil, are best avoided in patients with relevant risk factors, for example, lower potassium level, prolong electrical conduction within the heart of inborn, concomitant administration of medicinal used to decrease abnormal rhythms of the heart products (example quinidine, procainamide, amiodarone and sotalol).	within the heart during treatment with vardenafil, stop taking this medicine and contact your doctor/pharmacist/nurse immediately.
Prolonged erection, priapism	Vardenafil uncommonly prolonged erections in 1 out of 100 people and rarely cause painful erection in 1 out of 1,000 people.	Special care is needed if patient have an illness that can prolonged erection of the penis and penis not return to its normal position. These include abnormality in the oxygen-carrying haemoglobin molecule in red blood cells and cancer of blood-forming cells from bone marrow.

Risk	What is known	Preventability
		Do not drink alcohol, as this drink can worse erection difficulties. If a patient develops prolonged erection during treatment with Vardenafil, stop taking this medicine and contact your doctor/ pharmacist/nurse immediately. Special care is needed ifpatient are using any other treatments for erection difficulties, including vardenafilorally disintegrating tablet.
Access to drug product without prescription	None	None
Concomitant medication CYP3A4 inhibitors like erythromycin, clarithromycin, ketoconazole, itraconazole, ritonavir and	Do not take Vardenafil if patient over 75 years of age and are taking ketoconazole or itraconazole, anti-fungal medicines and CYP3A4 enzyme inhibitors because plasma concentrations of vardenafil is increased.	Patient should inform to doctor if they are taking any medicines like erythromycin, clarithromycin, ketoconazole, itraconazole, ritonavir and indinavirbefore starting the treatment with vardenafil.

Risk	What is known	Preventability
indinavir. (Cytochrome P450 3A4 (CYP3A4), is an important enzyme in the body, oxidize small foreign organic molecules (xenobiotics), such as toxins or drugs, so that they can be removed from the body) (risk of overdose)	Do not take Vardenafil if patient taking ritonavir or indinavir, medicines used to treat human immunodeficiency virus (HIV) infections and very potent inhibitors of CYP3A4 enzyme. Co-administration of indinavir with vardenafil (10 mg film-coated tablet) 7-fold increase in vardenafil concentration. Co-administration of ritonavirwith vardenafil (5 mg film-coated tablet) resulted in a 13-fold increase in vardenafil concentration. Don't drink grapefruit juice a weak inhibitor of CYP3A4 gut wall metabolism, may give rise plasma levels of vardenafil.	
Concomitant use with medicine used to treat high blood pressure and enlargement of the prostate.	The concomitant use to treat high blood pressure and enlargement of the prostate (tamsulosin or terazosin) and vardenafil may cause symptoms of decreasing blood pressure in some patients because both medicines widening	Always tell your doctor or pharmacist if you are taking any of these medicines that are often used to treat high blood pressure and enlargement of the prostate before starting the

Risk	What is known	Preventability
(Concomitant use of alpha-blockers) (risk of hypotension - decreased in blood pressure)	blood vessels. Therefore, concomitant treatment should be initiated only if the patient is stable on medicine. (Used to treat high blood pressure and enlargement of the prostate).	treatment with vardenafil.
Concomitant medication nitrates or NO donors (risk of hypotension – decreased in blood pressure)	Do not take vardenafil if patient taking medicines containing nitrates, such as glycerol trinitrate for angina, or nitric oxide donors, such as amyl nitrite. Taking these medicines with vardenafil could seriously affect your blood pressure.	You should not take Vardenafil tablets if you are taking medicines called nitrates, as the combination of these products may cause a potentially dangerous decrease in your blood pressure. Always tell your doctor or pharmacist if you are taking any of these medicines that are often used for the relief of angina pectoris (or “chest pain”). You should not take vardenafil tablets if you are using any of the drugs known as nitric oxide donors such as amyl nitrite as the combination may also lead to a potentially dangerous decrease in your blood pressure.

Risk	What is known	Preventability
Counterfeit drug product	None	None

Important potential risks

Risk	What is known
A condition involving loss of vision due to damage to the optic nerve from insufficient blood supply known as non arteritic ischemic optic neuropathy (NAION)	Do not take vardenafil tablets, if patient have ever had loss of vision due to non-arteritic anterior ischaemic optic neuropathy (NAION). If patient experience partial, sudden, temporary or permanent decrease or loss of vision in one or both eyes, stop taking vardenafil tablets and contact your doctor immediately. Vardenafil uncommonly effects on vision, cause redness of the eye, effects on colour vision, eye pain and discomfort, light sensitivity in 1 out of 100 people.
Sudden, temporary episode of memory loss (Transient global amnesia)	Vardenafil rarely affect amnesiain 1 out of 100 people.
Epilepsy/Seizure/Convulsion	Vardenafil rarely affect seizure in 1 out of 100 people.
Eye disease which causes visual impairment, often temporary (Central serous	Patients uncommonly (up to 1 in 100 people) experience effects on vision; redness of the eye, effects on colour

Risk	What is known
retinopathy)	vision, eye pain and discomfort, light sensitivity
Sudden hearing loss (Sudden deafness)	If you experience sudden decrease or loss of hearing, stop taking vardenafil tablets and contact your doctor immediately
Transient and permanent vision loss	If patient experience sudden decrease or loss of vision, stop taking vardenafil and contact doctor immediately. If patient experience partial, sudden, temporary or permanent decrease or loss of vision in one or both eyes, stop taking vardenafil tablets and contact your doctor immediately. Vardenafil uncommonly effects on vision, cause redness of the eye, effects on colour vision, eye pain and discomfort, light sensitivity in 1 out of 100 people. Avoid driving or operating of any tools or machines, if patient vision is affected after taking this medicine,

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 minimizing 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 special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements can be found in Annexure 10 and Annexure 11 of this RMP.

These additional risk minimisation measures are for the following two safety concerns.

1. Counterfeit drug product

Risk minimisation measure(s) Patient Education Material: Brochure, Flyer and dedicated internet website called "Beware of Counterfeits". For further information, please see http://www.accord-healthcare.eu/counterfeits
Objectives and rationale: Patient awareness to prevent the use of counterfeit drugs
Summary description of main additional risks minimisation measures: • Awareness raising on dedicated internet website called "Beware of Counterfeits" • Support of EFPIA's Coding and Identification Initiative / Mass Serialization • Procedures for detecting and prosecuting manufactures of counterfeit drug product

2. Access to drug product without prescription

Risk minimisation measure(s) Patient Education Material: Brochure, Flyer and dedicated internet website called "Beware of Counterfeits". For further information, please see http://www.accord-healthcare.eu/counterfeits
Objectives and rationale: Patient awareness to reduce the access to drug product without prescription.
Summary description of main additional risks minimisation measures: • Awareness raising on dedicated internet website called "Beware of Counterfeits" • Procedures for detecting and prosecuting manufactures of counterfeit drug product

VI.2.6 Planned post authorisation development plan

No studies planned

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

Version	Date	Safety Concern	Comment
4.0	29 April 2017	No change in safety concern.	RMP has been updated as per Day 120 comments of Vardenafil Accord (AT/H/0652/001-003/DC).
3.0	03 February 2017	No change in safety concern.	Additional risk minimisation measures have been added as per authority's feedback email on draft Day 106 responses.
2.0	17 August 2016	RMP has been updated with below safety concerns: **Important identified risks:** Following Important identified risks have been modified: • An important identified risk "effects on QT-interval and cardiac rhythm"	The safety concerns and relevant sections have been changed based on Day 70 Preliminary assessment report of Vardenafil Accord (AT/H/0652/001-

Version	Date	Safety Concern	Comment
		has been updated as "effects on QT-interval and cardiac rhythm (arrhythmias). • An important identified risk "Prolonged erection has been updated as ""Prolonged erection, priapism" • An important identified risk "Concomitant medication CYP 3A4 inhibitors" has been updated as "Concomitant medication CYP 3A4 inhibitors (risk of overdose)" • An important identified risk "Concomitant medication alpha-blockers" has been updated as "Concomitant medication alpha-blockers (risk of hypotension) • An important identified risk "Concomitant medication nitrates or NO donors" has been updated as "Concomitant medication nitrates or NO donors (risk of hypotension). Following Important identified risks have been included: • Counterfeit drug product **Potential risks:** *Following potential risks have been*	003/DC) dated 19 April 2016.

Version	Date	Safety Concern	Comment
		modified: • Potential risk "Ocular adverse events : Non-Arteritic Ischemic Optic Neuropathy (NAION) has been modified as "NAION (Non-Arteritic Ischemic Optic Neuropathy). • Potential risk "Transient amnesia" has been modified as "Transient Global Amnesia". *Following potential risk has been added* • Transient and permanent vision loss *Following potential risks have been excluded* • Penile haemorrhage, haematospermia and haematuria • Cardiovascular disorder (including myocardial infarction, Angina pectoris, ventricular arrhythmia, hypertension, cerebrovascular haemorrhage, sudden cardiac death, transient ischaemic attack and unstable angina)	

Version	Date	Safety Concern	Comment
		Missing information *Following missing information have been excluded* • Use of vardenafil in patients with recent history of stroke or myocardial infarction • Use of vardenafil in patients with known hereditary degenerative retinal disorders such as retinitis pigmentosa • Use of vardenafil in patients with severe hepatic impairment • Use of vardenafil in patients with end stage renal disease requiring dialysis	