VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Benign prostatic hyperplasia (BPH) (an increase in size of the prostate that is not cancerous) is the most prevalent of all diseases in aging men. Approximately 25% of men between ages 40 to 79 years will suffer from BPH. There are approximately 36 million European men with BPH. It is estimated that 50% of men under the age of 60 who undergo surgery for BPH may have a heritable form of the disease. The first-degree male relatives of such patients have increased chances of approximately 4-fold of developing BPH. Although BPH is generally not a life threatening condition, it can have a marked effect on a patient's quality of life. Acute urinary retention (a lack of ability to urinate) is one of the most significant complications of long-term BPH. Surgical treatment carries a higher rate of deaths in men presenting with acute urinary retention compared to those presenting with symptoms alone.

VI.2.2 Summary of treatment benefits

No pivotal clinical efficacy and safety studies were conducted for Dutasteride 0.5 mg soft capsules considering this is a generic product. However, based on the available data from clinical studies and clinical experiences of several years with the originator products, dutasteride is an effective and generally well tolerated drug in the treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH) and reduces the risk of acute urinary retention and need for surgery in patients with moderate to severe symptoms of BPH.

VI.2.3 Unknowns relating to treatment benefits

The efficacy of dutasteride has been studied in male patients. However, there is not available safety information related with men with severe hepatic impairment and in men with unstable medical conditions such as recent myocardial infarction, coronary bypass surgery, unstable angina, cardiac arrhythmias, clinically evident congestive heart failure or cerebrovascular accident, cancer or uncontrolled diabetes or peptic ulcer disease.

VI.2.4 Summary of safety concerns

Important identified risks:

Risk	What is known	Preventability
Sexual adverse events ((altered [decreased] libido, impotence, ejaculation disorders) and breast disorders (enlargement and tenderness))	In several studies, altered [decreased] libido occurred in 3.7-3.8% of patients during the first year of treatment with dutasteride, in 0.6-1.0% in year 2, in 0.2% in year 3 and in 0% in year 4. Impotence occurred in 5.1-6.0% of patients during the first year of treatment with dutasteride, in 1.5- 1.7% in year 2, in 0.6% in year 3 and in 0.3% in year 4. Ejaculation disorders occurred in 1.5-1.8% of patients in year 1, in 0.5% in year 2, in 0.2% in year 3 and in 0.3% in year 4. Breast disorders (including breast enlargement and/or breast tenderness) occurred in 1.3-1.7% of patients in year 1, in 1.2-1.3% in year 2, in 0.5% in year 3 and in 0.7% in year 4.	During treatment or after treatment with dutasteride if patient experiences any of the stated sexual side effects, he should report promptly to the treating physician.
Allergic reactions (i.e. skin alterations) (Allergic reactions including rash, pruritus, urticaria, localised oedema, and angioedema)	Incidence estimated is unknown. Dutasteride is contraindicated in patients with hypersensitivity to dutasteride, other 5-ARIs, soya and peanut or to any of the excipients. This medicinal product contains lecithin (may contain soya oil).	**Do not take dutasteride** if you are allergic to dutasteride, other 5-alpha reductase inhibitors, soya, peanut or to any of the other ingredients of this medicine.

Risk	What is known	Preventability
	The signs of allergic reactions can include: - skin rash (which can be itchy) - hives (like a nettle rash) - swelling of the eyelids, face, lips, arms or legs.	
Heart failure (Cardiac failure)	It is an uncommon adverse reactioin (may affect up to 1 in 100 men): In several clinical studies, the incidence of cardiac failure was higher among subjects taking the combination of dutasteride and alpha blockers (specific group of drugs). The incidence of cardiac failure was low (≤1%) and variable between the studies.	During treatment or after treatment with dutasteride if patient experiences events other than cardiac failure, he should report promptly to the treating physician.
State of low mood and aversion to activity that can affect a person's thoughts, behaviour, feelings and sense of well-being (Depressed mood)	Frequency of depressed mood cannot be estimated from the available data. Depression could appear in susceptible patients. Specifically, it is described that finasteride treatment has been associated with an increase of depressive symptoms.	During treatment or after treatment with dutasteride if patient experiences any events regarding low mood, changes in behaviour, feelings and sense of well-being, he should report promptly to the treating physician.

Important potential risks:

Risk	What is known
Heart and vascular events other than heart failure (Cardiovascular events other than cardiac failure)	Among two specific studies (CombAT and REDUCE) no imbalance or significant difference between the dutasteride and placebo group was observed in the incidence of overall cardiovascular adverse events or deaths. The REDEEM study showed no increase in cardiovascular adverse events with dutasteride treatment.
Male breast cancer	*Breast neoplasia* Breast cancer has been reported in men taking dutasteride in clinical trials and during the post-marketing period. Physicians should instruct their patients to promptly report any changes in their breast tissue such as lumps or nipple discharge. Currently it is not clear if there is a causal relationship between the occurrence of male breast cancer and long term use of dutasteride.
High-grade prostate cancer	Results of one clinical study (REDUCE) in men at increase risk of prostate cancer revealed a higher incidence of Gleason 8 – 10 prostate cancers (high-grade prostate cancer) in dutasteride treated men compared to placebo. The relationship between dutasteride and high grade prostate cancer is not clear. Men taking dutasteride should be regularly evaluated for prostate cancer risk including PSA testing.
Interference with formation of external male genitalia in the foetus	Dutasteride has been found in the semen of men taking dutasteride. Thus, owing to the mode of action of dutasteride, if it is administered to a woman carrying a male foetus, may inhibit the normal development of foetus.

Missing information:

Risk	What is known
Men patients with decreased liver function (Men with severe hepatic impairment)	Dutasteride has not been studied in patients with liver disease. Therefore, special care should be taken in patients with mild to moderate loss of liver functioning. In patients with severe loss of liver functioning, the use of dutasteride is contraindicated.

Risk	What is known
Men with unstable medical conditions (Men with unstable medical conditions such as recent myocardial infarction, coronary bypass surgery, unstable angina, cardiac arrhythmias, clinically evident congestive heart failure or cerebrovascular accident, cancer or uncontrolled diabetes or peptic ulcer disease).	No specific data are available currently.

VI.2.5 Summary of additional risk minimization measures by safety concern

Summary of Product Characteristics (SmPC) of Dutasteride 0.5 mg soft capsules 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). All these risk minimization measures are given in SmPC and PL of Dutasteride 0.5 mg soft capsules.

This medicine has no additional risk minimization measures.

VI.2.6 Planned post authorisation development plan

Neither planned studies nor studies imposed by the Committee for Medicinal Products for Human Use (CHMP)/National Competent Authorities (NCA) are foreseen for the aforementioned product. Therefore, there is no need to perform with post-authorisation efficacy studies (PAES) or post-authorisation safety studies (PASS).

List of studies in post authorisation development plan

Not applicable.

Studies which are a condition of the marketing authorisation

Not applicable.

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

Version	Date	Safety Concerns	Comment
01	11/April/2014	**Important identified risks:** Reproductive systems - Sexual adverse events of altered [decreased] libido, impotence, ejaculation disorders) that may persists after drug discontinuation. - Breast disorders (enlargement and tenderness). -Allergic reactions, including rash, pruritus, urticaria, localised oedema, and angioedema -Cardiac failure -Depressed mood **Important potential risks:** -Cardiovascular events other than cardiac failure -Male breast cancer -High-grade prostate cancer -Interference with formation of external male genitalia in the foetus **Important missing information:** Safety of dutasteride therapy in: -Men with severe hepatic impairment	This version was updated according to RMS Day 70 Draft Assessment Report 13/Jul/2015.

Version	Date	Safety Concerns	Comment
		-Men with unstable medical conditions such as recent myocardial infarction, coronary bypass surgery, unstable angina, cardiac arrhythmias, clinically evident congestive heart failure, or cerebrovascular accident; cancer; or uncontrolled diabetes or peptic ulcer disease.	
1.1	28 Sept. 2015	None. Minor comment have been updated in table VI. 2.4	This version was updated according to RMS Day 120 Draft Assessment Report 04/Jan/2016.