VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Prostate gland enlargement is a common condition as men get older. Also called benign prostatic hyperplasia (BPH) and prostatic hypertrophy, prostate gland enlargement can cause bothersome urinary symptoms. Untreated prostate gland enlargement can block the flow of urine out of the bladder and can cause bladder, urinary tract or kidney problems. BPH is quite common, affecting roughly 50% of men between ages 50 and 60.

VI.2.2 Summary of treatment benefits

Based on the available data from clinical studies and clinical experience of several years, dutasteride represents an effective drug in the treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH) and reduction in the risk of acute urinary retention and surgery in patients with moderate to severe symptoms of BPH.

If administered as indicated in the Summary of Product Characteristics and taking into account the contra-indications, the warnings and precautions, dutasteride can be considered effective in the approved indications and generally well tolerated.

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
Sexual adverse events (altered (decreased) libido, impotence, ejaculation disorders, that may persist after discontinuation of drug) and breast disorders (enlargement and tenderness)	Dutasteride has been shown to commonly cause problems with erection and ejaculation, and decreases sex drive. Dutasteride may cause breast enlargement and tenderness.	Treating physicians and patients should be aware of the risk.
Allergic reactions, including rash, pruritus, urticaria, localised oedema and angioedema	Very rare allergic reactions have been noticed with dutasteride therapy. 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.	Dutasteride should not be used in patients who have known allergies to dutasteride. If any of the symptoms appear, medicine should be stopped immediately and the doctor should be contacted.
Heart failure (Cardiac failure)	In some clinical studies, more patients taking dutasteride and another medicine called an alpha blocker, like tamsulosin, experienced heart failure than patients taking only dutasteride or only an alpha blocker. Heart failure means your heart does not pump blood as well as it should. Heart failure may affect up to 1 in 100 men taking dutasteride.	Symptoms such as shortness of breath, extreme tiredness and swelling in ankles and legs could be signs of heart failure. Patient are advisd to talk to their doctor before taking dutasteride.
Depressed mood	Depressed mood is a possible side effect with dutasteride.	Patients are advised to tell their doctor or pharmacist if any of the side effects get serious.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Disorders of heart and blood vessels (Cardiovascular events (other than cardiac failure))	Dutasteride may potentially cause heart disorders other than heart failure.
Male breast cancer	Breast cancer has been reported in men taking dutasteride in some clinical trials. Currently it is not clear if there is a causal relationship between the occurrence of male breast cancer and

Risk	What is known (Including reason why it is considered a potential risk)
	long term use of dutasteride. However, dutasteride may cause breast enlargement and tenderness. If breast lumps or nipple discharge appear, the doctor should be consulted as these may be signs of a serious condition, such as breast cancer.
High-grade prostate cancer	In a clinical study of men at increased risk of prostate cancer, men taking dutasteride had a serious form of prostate cancer more often than men who did not take dutasteride. The effect of dutasteride on this serious form of prostate cancer is not clear. Men taking dutasteride should have their prostate-specific antigen (PSA) tested regularly. Dutasteride affects a blood test for PSA, which is sometimes used to detect prostate cancer; prior to tests doctors should be warned about the dutasteride therapy.
Effect on development of external genital organs in male babies (Interference with formation of external male genitalia in the foetus)	Dutasteride must not be used by women. Dutasteride has been found in the semen of men taking dutasteride. Pregnant women must not be exposed to semen of the partner taking dutasteride as dutasteride may affect the normal development of a male baby. Condom must be used during sexual intercourse. Also, (pregnant) women must not handle leaking dutasteride capsules, because the active ingredient can be absorbed through the skin.

Important missing information

Risk	What is known
Men with severe liver function problems (Men with severe hepatic impairment)	Dutasteride must not be taken if severe problems with liver function exist. Caution should be used in the administration of dutasteride to patients with mild to moderate liver impairment. Patients who have had any illness affecting liver may need regular monitoring while taking dutasteride. Dutasteride was not studied in patients with liver disease.
Men with different serious and unstable illnesses (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 data are available on dutasteride use in men with unstable medical conditions.

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

No additional risk minimisation measures are proposed.

VI.2.6 Planned post authorisation development plan (if applicable)

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	29 May 2013	**Important identified risks** • Sexual adverse events (altered [decreased] libido, impotence, ejaculation disorders) and breast disorders (enlargement and tenderness) • Allergic reactions, including rash, pruritus, urticaria, localised oedema, and angioedema **Important potential risks** • Male breast cancer • Cardiovascular events • High-grade prostate cancer • Interference with formation of external male genitalia in the foetus **Missing information** • Men with severe hepatic impairment • Men with unstable medical conditions	Not applicable.
1.1	25 November 2013	**Important identified risks** • Sexual function disturbances • Allergic reactions **Important potential risks** • Reduced male fertility • Male breast cancer • Cardiac failure (in combination therapy with alpha-blocker) • High-grade prostate cancer • Interference with formation of external male genitalia in the foetus **Missing information** • Men with severe hepatic impairment • Men with unstable medical conditions	Risk “Sexual adverse events (altered [decreased] libido, impotence, ejaculation disorders) and breast disorders (enlargement and tenderness)“ has been changed to “Sexual function disturbances”, and “Allergic reactions, including rash, pruritus, urticaria, localised oedema, and angioedema” to “Allergic reactions” Risk “Reduced male fertility”, previously described as part of the risk “Sexual adverse events…” has been added as important potential risk Risk “Cardiovascular events “ has been changed to “Cardiac failure (in combination therapy with alpha-blocker)”

Version	Date	Safety Concerns	Comment
1.2	10 January 2014	Unchanged	Tables in part III.1 were updated to include previously proposed risks. Table in part V.1 was amended to include information on follow-up questionnaire in male breast cancer and high grade prostate cancer.
2.0	16 March 2016	**Important identified risks** • Sexual adverse events (altered (decreased) libido, impotence, ejaculation disorders, that may persist after discontinuation of drug) and 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 **Missing information** • Men with severe hepatic impairment • 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	All parts of RMP were amended to reflect the proposed list of safety concerns in order to align with the RMP for other products containing the same substance for the same indication. Since the v1.2 was already approved in another procedure, the new version stated is 2.0.