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 a 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)	Frequency of allergic reactions cannot be estimated from the available data. Dutasteride contains lecithin (may contain soya oil). It is contraindicated in patients with hypersensitivity to dutasteride, other 5-ARIs, soya and peanut or to any of the excipients. Incidence of allergic reactions is unknown. Signs of allergic reaction include skin rash (can be itchy), hives (like nettle rash), swelling of eyelids, face, lips, arms or legs.	Patients who are allergic to dutasteride, other 5-alpha reductase inhibitors, soya, peanut or to any of the other ingredients of this medicine should not take dutasteride. During treatment or after treatment with dutasteride if a patient experiences allergic reactions, he should report promptly to the treating physician.

Heart failure (Cardiac failure)	Combination therapy (dutasteride and alpha blocker) should be prescribed carefully. 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 a patient experiences heart problems, 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.	During treatment or after treatment with dutasteride if patient experiences low mood, he should report promptly to the treating physician.

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Heart and vascular events other than heart failure (Cardiovascular events other than cardiac failure)	Among two specific studies no imbalance or significant difference between the dutasteride and placebo group was observed in the incidence of overall cardiovascular adverse events or deaths. Other 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	Dutasteride affects a blood test for PSA (prostate-specific antigen), which is sometimes used to detect prostate cancer. Physicians should be aware of this effect. Men having a blood test for PSA should inform their doctor that they are taking dutasteride. They should have their PSA tested regularly. 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 it. The effect of dutasteride on this serious form of prostate cancer is not clear.
Interference with formation of external male genitalia in the foetus	Dutasteride is contraindicated in women, children and adolescents. 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 function. In patients with severe loss of liver function, the use of dutasteride is contraindicated.
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 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.

The Summary of Product Characteristics and the Package leaflet for this product can be found at the agency's EPAR page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable. No postauthorisation studies are planned.

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

Not applicable, this is the first Risk management plan.