

## VI.2 Elements for a Public Summary

### VI.2.1 Overview of disease epidemiology

Benign prostatic hyperplasia (BPH) 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. Approximately 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 (AUR) is one of the most significant complications of long-term BPH. Surgical treatment carries a higher rate of deaths in men presenting with AUR compared to those presenting with symptoms alone. [Roehrborn, 2001; Fong 2004; Shrivastava and Gupta 2012; Presti, 2012]

### 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. The available medical literature is considered sufficient to evaluate the safety of Dutasteride 0.5 mg soft capsules in the proposed therapeutic indication.

### VI.2.3 Unknowns relating to treatment benefits

Dutasteride has not been studied in patients with liver disease. Therefore special care should be taken in patients with mild to moderate hepatic impairment. The relationship between dutasteride and high grade prostate cancer is not clear. Men taking dutasteride should be regularly evaluated for prostate cancer risk including prostate-specific antigen (PSA) testing. Currently it is not clear if there is a causal relationship between the occurrence of male breast cancer and long term use of dutasteride.

### VI.2.4 Summary of safety concerns

#### Important Identified Risks

Risk	What is known	Preventability
<b>Sexual side effects like man's inability to have or maintain an erection of his penis, decreased sex drive, difficulty with ejaculation, that may</b>	In clinical trials with dutasteride alone or dutasteride in combination with another medicine called tamsulosin, the sexual side effects like erectile dysfunction, libido disorder, and ejaculation disorder have been	Yes, during treatment or after treatment with dutasteride if patient experience any of the stated sexual side effects he should report promptly to their doctor.

Risk	What is known	Preventability
<p><b>persist after discontinuation of drug.</b> <b>(Sexual adverse events (altered [decreased] libido, impotence, ejaculation disorders), that may persist after discontinuation of drug)</b></p>	<p>reported in significant number of patients treated with dutasteride.</p>	
<p><b>Breast disorders (enlargement and tenderness)</b></p>	<p>In clinical trials with dutasteride alone or dutasteride in combination with another medicine called tamsulosin, the sexual side effects like breast disorders (enlargement and tenderness) have been reported in significant number of patients treated with dutasteride.</p>	<p>Yes, during treatment or after treatment with dutasteride if patient experience any of the breast disorder (enlargement and tenderness) sexual side effects he should report promptly to their doctor.</p>
<p><b>Allergic reactions, including rash, severe itching of the skin (pruritus), raised, itchy rash that appears on the skin (urticarial), localised fluid retention (localised oedema), and swelling of the deeper layers of the skin, caused by a build up of fluid (angioedema)</b></p>	<p>The following adverse reactions from controlled trials (with dutasteride alone or dutasteride in combination with another medicine called tamsulosin) and post-marketing experience were reported in patients treated with dutasteride:</p> <p>Allergic reaction, including:</p> <ul style="list-style-type: none"> <li>• Rash</li> <li>• Pruritus (severe itching of the skin)</li> <li>• Urticarial (also known as hives, is a raised, itchy rash that appears on the skin)</li> <li>• Localised oedema (fluid retention)</li> <li>• Angioedema (swelling of the deeper layers of the skin, caused by a build-up of fluid)</li> </ul>	<p>Yes, during treatment or after treatment with dutasteride if patients experience any of the below side effect, they are advised to report to their doctor:</p> <p>Allergic reaction, including:</p> <ul style="list-style-type: none"> <li>• Rash</li> <li>• Pruritus (severe itching of the skin)</li> <li>• Urticarial (also known as hives, is a raised, itchy rash that appears on the skin)</li> <li>• Localised oedema (fluid retention)</li> </ul>

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
<b>Inability of heart to pump blood sufficiently (Cardiac failure)</b>	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.	Yes, patient having any heart related problem should inform to treating physician prior to start of treatment. Patient history for cardiac failure should be taken and doctor should inform patient about this risk before start of the therapy.
<b>Depressed mood</b>	The depressed mood adverse reaction from controlled trials (with dutasteride alone or dutasteride in combination with another medicine called tamsulosin) and post-marketing experience were reported in patients treated with dutasteride:	Yes, like all medicines, this medicine can cause side effects, although not everybody gets them.  Not known side effects Frequency cannot be estimated from the available data which include: <ul style="list-style-type: none"> <li>depressed mood</li> </ul>

**Important potential risks:**

<b>Risk</b>	<b>What is known</b>
<b>Cardiovascular events (other than cardiac failure)</b>	In some clinical studies, more patients taking dutasteride and another medicine called an alpha-blocker, like tamsulosin, experienced cardiovascular events than patients taking only dutasteride or only an alpha blocker.
<b>Cancer of breast in men (Male breast neoplasia)</b>	In a clinical trial, 2 cases of breast cancer in men were reported in dutasteride-treated patients and 1 case in a patient who received placebo.
<b>High grade prostate cancer</b>	Men taking dutasteride should be regularly evaluated for prostate cancer risk including prostate-specific antigen (PSA) testing.
<b>Obstruction in the normal development of unborn male child (Interference with formation of external male genitalia of the foetus)</b>	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:**

<b>Risk</b>	<b>What is known</b>
<b>Men with severe loss of liver function (Men with severe hepatic impairment)</b>	Dutasteride has not been studied in patients with liver disease. Therefore special care should be taken in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, the use of dutasteride is contraindicated.
<b>Men with unstable medical conditions such as recent heart attack (myocardial infarction), surgery to treat coronary heart disease (coronary bypass surgery unstable angina), irregular heartbeat (cardiac arrhythmias), clinically evident disorder of the heart chambers (congestive heart failure), or stroke (cerebrovascular accident); cancer, or uncontrolled diabetes or stomach ulcer (peptic ulcer disease).</b>	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. Cardiac failure composite term comprised of Cardiac failure congestive, cardiac failure, left ventricular failure, cardiac failure acute, cardiogenic shock, left ventricular failure acute, right ventricular failure, right ventricular failure acute, ventricular failure, cardiopulmonary failure, congestive cardiomyopathy. The relationship between dutasteride and high grade prostate cancer is not clear. Men taking dutasteride should be regularly evaluated for prostate cancer risk including prostate-specific antigen (PSA) testing. Currently it is not clear if there is a causal relationship between the occurrence of male breast cancer and long term use of dutasteride.

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

Summary of Product Characteristics (SPC) 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 SPC 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**

Dutasteride 0.5 mg soft capsules are approved in Spain since 2003. After authorization the Spain regulatory has not asked for any development plan and the applicant has not planned the same post-authorization.

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

Version	Date (dd-mm-yyyy)	Safety Concerns	Comment
02	15.03.2016	<p>The below safety concerns have been added as suggested by agency comments:</p> <p><u>Important Identified risk</u></p> <ul style="list-style-type: none"> <li>- Sexual adverse events (altered [decreased] libido, impotence, ejaculation disorders), that may persist after discontinuation of drug.</li> <li>- Breast disorders (enlargement and tenderness)</li> <li>- Allergic reactions, including rash, pruritus, urticarial, localised oedema, and angioedema</li> <li>- Cardiac failure</li> <li>- Depressed mood</li> </ul> <p><u>Important Potential Risks</u></p> <ul style="list-style-type: none"> <li>- Cardiovascular events (other than cardiac failure)</li> <li>- Male breast cancer</li> <li>- High grade prostate cancer</li> <li>- Interference with formulation of external male genitalia in the foetus</li> </ul> <p><u>Missing Information</u></p> <ul style="list-style-type: none"> <li>- Men with severe hepatic impairment</li> <li>- 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.</li> </ul>	As per agency suggestion