VI.2 ELEMENTS FOR A PUBLIC SUMMARY

VI.2.1 Overview of Disease Epidemiology

The prostate is a gland that is found only in males. This gland is near the bladder, and it normally makes the fluid which carries sperm. It is common for the gland to become bigger as a man ages. This increase in size does not usually cause problems until late in life. This condition is called benign prostatic hyperplasia (BPH).

Only about half of men who have BPH have symptoms. Such symptoms are sometimes called Lower Urinary Tract Symptoms (LUTS). LUTS can include: dribbling at end of urinating, slow start of urinating, weak urinating, not being able to urinate, incomplete urinating, leaking urine, need for night urinating multiple times, strong and sudden urge to urinate, pain when urinating, or blood in urine.

The cause of BPH is not known. However, men who have one or more risk factors have a higher chance of having BPH and LUTS. These risk factors include:
- increased age
- family history of BPH
- changeable lifestyle (including lack of physical activity, being overweight or obese)
- a body process called inflammation (which often results from infections of many types).

Because increased age is a risk factor for BPH and LUTS, these conditions are more common in older men than in younger men. In older men, BPH is quite common – more than 90% of men over age 80 years have BPH. BPH is more common in Western countries than in Asian or Eastern countries.

The percentage of men with BPH seems to be increasing over time. In the US, this percentage rose from about 4% in 1998 to 8% in 2008. However, at least part of that increase is because the percentage of older men in the overall population has also increased over time.

VI.2.2 Summary of Treatment Benefits

PROSCAR is prescribed for individuals with benign prostatic hyperplasia.

PROSCAR shrinks the enlarged prostate and relieves urinary symptoms. PROSCAR will help reduce the risk of developing a sudden inability to pass urine (acute urinary retention) and the need for surgery for BPH.

The main studies of PROSCAR looked at 536 patients with symptoms of BPH and enlarged prostates in two 1-year studies that continued through five 1-year extensions. A total of 236 of these patients completed 5-year study extensions. In these studies, average total urinary symptom scores improved after 2 weeks of treatment. Compared with placebo (sugar pill), a significant improvement in symptoms was seen by months 7 and 10 in these studies. At least 6 months of treatment was generally needed for improvement of urinary symptoms. The improvement in BPH symptoms continued through the first year and throughout the additional 5 years of study extensions.

In the PROSCAR Long-Term Efficacy and Safety Study (PLESS), the effect of therapy with PROSCAR on BPH-related urinary events (such as the need for surgery on the prostate] or sudden inability to urinate) was examined over a 4-year period in 3040 patients with moderate to severe symptoms of BPH. In this study, treatment with PROSCAR reduced the risk of urinary events by 51% and was also associated with a decrease in the size of the prostate, and improvement of urinary symptoms.

VI.2.3 Unknowns Relating to Treatment Benefits

The effect of hepatic insufficiency on the pharmacokinetics of finasteride has not been studied. Finasteride is metabolized in the liver. Caution is recommended in patients with impaired hepatic function as the plasma concentration of finasteride may increase in these patients.

VI.2.4 Summary of Safety Concerns

Important Identified Risks

Table 42 Summary of Important Identified Risks

Risk	What is Known	Preventability
Contact with PROSCAR by oral use or through the skin during Pregnancy	If a woman who is pregnant with a male baby absorbs the active ingredient in PROSCAR after oral use or through the skin, it may cause the male baby to be born with abnormalities of the sex organs.	Women who are or may potentially be pregnant must not use PROSCAR. They should also not handle crushed or broken tablets of PROSCAR. PROSCAR tablets are coated and will prevent contact with the active ingredient during normal handling as long as the tablets are not broken or crushed. If a women who is pregnant comes in contact with the active ingredient in PROSCAR, a doctor should be consulted.
Off-label use in women and adolescents	Benign Prostatic Hyperplasia, the condition for which PROSCAR is indicated, occurs in adult males. Therefore PROSCAR is not indicated for use in women or children. In addition, based on the mechanistic effects of finasteride on the development of the external genitalia of the developing male fetus, the use of finasteride in women who are or may potentially be pregnant is contraindicated. As noted above, the condition for which PROSCAR is indicated does not occur in children and PROSCAR has not been studied in children	The following sections of the label provide clear information on the use of finasteride **Contraindications**: PROSCAR is not indicated for use in women or children. This section also clearly states that: PROSCAR is contraindicated in Pregnancy - Use in women when they are or may potentially be pregnant (See PRECAUTIONS: PREGNANCY and EXPOSURE TO FINASTERIDE - RISK TO MALE FETUS). **Pediatric use**. PROSCAR is not indicated for use in children

Table 42 Summary of Important Identified Risks

Risk	What is Known	Preventability
	PROPECIA (finasteride 1 mg) is indicated for the treatment of men with male pattern hair loss (androgenetic alopecia) to increase hair growth and prevent further hair loss. It is possible that PROSCAR may be prescribed for off-label use in women and adolescents with hair loss. However, both the PROSCAR and PROPECIA labels indicated that the drug is **not** indicated for use in women or children and it is contraindicated in women when they are or may potentially be pregnant	Safety and effectiveness in children have not been established The information for the patient clearly states that women and children should not take PROSCAR.

Important Potential Risks

Table 43 Summary of Important Potential Risks

Risk	What is Known
Problems with sexual function (inability to have an erection, problems with ejaculation, decreased sex drive) which may continue after stopping the medication	Problems with sexual function (inability to have an erection, problems with ejaculation, decreased sex drive) which may continue after stopping the medicine have been reported with use of marketed PROSCAR
Male Infertility	Male infertility and/or poor quality of the semen has been reported during use of PROSCAR (frequency unknown). Normalization or improvement in the quality of the semen has been reported after stopping the medication.
Depressive Disorders	Depressive disorders have been reported during postmarketing use of PROSCAR (frequency unknown); however, causal association with PROSCAR therapy has not been established.
Male Breast Cancer	Male breast cancer has been reported in men taking PROSCAR during clinical trials and in postmarketing use. The relationship between long-term use of finasteride and male breast cancer is currently unknown.

Missing Information

Table 44 Summary of Missing Information

Missing Information	What is Known
None	

VI.2.5 Summary of Risk Minimization 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, along with the risks of the medicine and recommendations for minimizing these risks. 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 minimization measures.

The UK Summary of Product Characteristics and the Package Leaflet for PROSCAR can be found in the product's eMC (electronic Medicines Compendium) page.

This medicine has no additional risk minimization measures.

VI.2.6 Planned Post-authorization Development Plan

VI.2.6.1 List of Studies in Post-authorization Development Plan

Table 45 List of Studies in Post-Authorization Development Plan

Study / Activity (including study number)	Objectives	Safety Concern(s) / Efficacy Issue(s) Addressed	Status	Planned Date for Submission of (Interim and) Final Results
A multinational, observational registry-based study on a potential link between finasteride and male breast cancer in 4 Nordic countries (Study #1, Stage #1)	Determine if male breast cancer occurs more often in men who have used finasteride than in men who have not used finasteride.	Male breast cancer	Completed	Interim report completed: 16-NOV-2012
Finasteride and male breast cancer – a register-based nested case-control study in Denmark, Finland, Norway and Sweden (Study #1, Stage # 2)	Determine what factors might make male breast cancer *appear* to occur more often in finasteride users than in finasteride non-users, assuming finasteride does not cause male breast cancer. Sometimes, a disease might appear to occur more often in one group of persons than another group of persons, but the actual cause of the disease is equally present in both groups.	Male breast cancer	Ongoing	The target completion date of report is 2Q2018

VI.2.6.2 Studies Which are a Condition of the Marketing Authorization

The above study is not a condition of the marketing authorization.

VI.2.7 Summary of Changes to the Risk Management Plan Over Time

Table 46 Major Changes to the Risk Management Plan

RMP Version	Date	Safety Concerns	Comment
1.0	**31-DEC-2009**	**Summary—Ongoing Safety Concerns** **Important Identified Risks** Contact with PROSCAR by oral use or through the skin during Pregnancy Women and children 12-17 years old taking PROSCAR **Important Potential Risks** Inability to have an erection, which may continue after stopping the medication Male Infertility Depression Male Breast Cancer **Important Missing Information** None	
2.0	**07-OCT-2013**	No changes to the safety concerns	The focus of the update to this version of the RMP (2.0) was to include current information about the male breast cancer study
3.0	**07-AUG-2015**	**No changes to the safety concerns**	The main focus of this update to this version of the RMP (3.0) was to include current information about the male breast cancer study
4.0	**14-OCT-2016**	**No changes to the safety concerns**	The main focus of this update to this version of the RMP (4.0) was to include current information about the male breast cancer study
4.1	**25-APR-2017**	**Important Potential Risks** Problems with sexual function (inability to have an erection, problems with ejaculation, decreased sex drive) which may continue after stopping the medication	The potential risk of Inability to have an erection, which may continue after stopping the medication, was updated to Problems with sexual function (inability to have an erection, problems with ejaculation, decreased sex drive) which may continue after stopping the medication.