Summary of Risk Management Plan for PROPECIA

This is a summary of the risk management plan (RMP) for finasteride 0.2[a] and 1 mg. The RMP details important risks of finasteride 0.2 and 1 mg, how these risks can be minimized, and how more information will be obtained about the risks and uncertainties (missing information) for finasteride 0.2 and 1 mg.

The summary of product characteristics (SmPC) and package leaflet for finasteride 1 mg give essential information to healthcare professionals and patients on how finasteride 1 mg should be used.

Any important new safety concerns will be included in future updates to the finasteride 0.2 and 1 mg RMP.

I. The Medicine and What it is Used for

In the EEA, PROPECIA is authorised in men 18-41 years of age for the early stages of androgenetic alopecia. PROPECIA stabilizes the process of androgenetic alopecia. (see SmPC for the full indication). It contains finasteride as the active substance and it is given orally.

II. Risks Associated With the Medicine and Activities to Minimize or Further Characterise the Risks

Important risks of finasteride 0.2 and 1 mg, together with measures to minimize such risks and the proposed studies for learning more about finasteride's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

[a] Finasteride 0.2 mg is not available in the EEA.

Together, these measures constitute *routine risk minimisation* measures.

In the case of finasteride 0.2 and 1 mg, these measures are supplemented with additional risk minimisation measures mentioned under the relevant important risk, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed including PSUR assessment that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of Important Risks and Missing Information

Important risks of finasteride 0.2 and 1 mg are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of finasteride 0.2 and 1 mg. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table II.A.1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	• Suicidal ideation • Sexual dysfunction (decreased libido, erectile dysfunction and ejaculation disorders) • Depressive disorders
Important potential risks	None
Missing information	None

II.B Summary of Important Risks

Table II.B.1.1: Important Identified Risk: Suicidal ideation

Evidence for linking the risk to the medicine	Although a causal relationship has not been established between PROPECIA and suicidal ideation, it may have a meaningful impact on the individual patient.
Risk factors and risk groups	Multiple domains of risk factors have been identified as contributing to suicidal behavior and ideation. Family-related factors include

Table II.B.1.1: Important Identified Risk: Suicidal ideation

	dysfunction, negative parenting styles, parental absence, poor communication, and lack of parental protection, as well as exposure to domestic violence and a negative paternal role. Biological factors such as a personal or family history of suicide attempts, age, and female gender have also been associated with increased vulnerability. Psychological factors encompass mental health disorders—including depression, anxiety, and eating disorders—along with stressful life events, low self-esteem, hopelessness, and substance use (alcohol, tobacco, and marijuana). Social determinants play a significant role, with bullying, romantic breakups, partner infidelity, exposure to violence, limited educational opportunities, sexual violence, and poor academic performance being strongly linked to risk. Additionally, self-harm behaviors and issues related to sexual orientation are highly predictive. Spiritual factors, such as not practicing any religion or certain religious affiliations, have shown smaller but notable associations with suicidal behavior [Ref. 5.4: 0FLW2L]
Risk minimisation measures	Routine risk minimisation measures : SmPC Section 4.4 (Suicidal ideation) recommends monitoring patients for psychiatric symptoms. Suicidal ideation is addressed in SmPC Section 4.8 Undesirable effects. Additional risk minimisation measures: A patient card will be provided inside the medication box for each patient. The risk is addressed as suicidal thoughts through this patient card, which offers clear information to patients on recognizing symptoms and seeking timely medical advice. The risk is addressed through the Direct Healthcare Professional Communication (DHPC), which delivers targeted guidance to prescribers and other healthcare professionals to ensure appropriate monitoring and management.

Table II.B.1.2: Important Identified Risk: Sexual Dysfunction (Decreased Libido, Erectile Dysfunction and Ejaculation Disorders).

Evidence for linking the risk to the medicine	Although a causal relationship has not been established between PROPECIA and sexual dysfunction after discontinuation of the medication, sexual dysfunction may have a meaningful impact on the individual patient.
Risk factors and risk groups	The prevalence of male sexual dysfunction increases with age and is relatively high with greater than 50% of men aged 40 to 70 describing some degree of erectile dysfunction. Risk factors for male sexual dysfunction include age, diabetes mellitus (DM), cancer, stroke, hypertension, penile trauma, depression, anxiety, and disturbance in central serotonin neurotransmission and 5-HT postsynaptic receptor functioning [Ref. 5.4: 0FLXBV]. One finding of this study was a 10-fold difference in relative risk for erectile dysfunction associated with older age. Comorbid conditions, such as diabetes mellitus, cancer, stroke, and hypertension, were associated with increased risk for erectile dysfunction. The two most common diseases that can cause erectile dysfunction are atherosclerosis and diabetes. Lifestyle habits such as smoking and alcohol use as well as comorbid conditions like obesity can also cause hypogonadism and hormonal changes that can lead to erectile dysfunction. Diseases that impair the nervous system, such as multiple sclerosis and Parkinson disease, injuries to the spinal cord can also disrupt these neural pathways and certain medications and recreational drugs like antihypertensives, anti-androgens, anticholinergics, psychotropic agents, narcotics, marijuana, and alcohol have been shown to cause erectile dysfunction [Ref. 5.4: 0FLXBV]. Decreased Libido is a multifactorial condition influenced by biological, psychological, relational, and cultural factors. Psychological contributors include negative sexual cognitions, anxiety, relationship dissatisfaction, and emotional distress. Biologically, testosterone

Table II.B.1.2: Important Identified Risk: Sexual Dysfunction (Decreased Libido, Erectile Dysfunction and Ejaculation Disorders).

	plays a role but circulating levels do not always correlate directly with desire, especially in older men. Other biological factors implicated include thyroid dysfunction, hyperprolactinemia, depression, and chronic illnesses such as cardiovascular disease and diabetes. Risk factors identified in large international surveys include older age (60-80 years), poor overall health, vascular diseases, smoking, recent divorce, financial stress, depression, and low frequency of sexual activity [Ref. 5.4: 0FLXCK]. Ejaculation disorders encompass a spectrum of conditions including premature ejaculation (PE), delayed ejaculation (DE), anejaculation, painful ejaculation, retrograde ejaculation, anorgasmia, and haemospermia. PE is the most common ejaculatory disorder with a prevalence varying widely due to differing definitions, and its pathophysiology involves psychological and biological factors such as anxiety, penile hypersensitivity, and serotonergic dysfunction. DE is less common, with a prevalence around 3-4%, and can be caused by psychological, organic, or pharmacological factors. Anejaculation is characterized by the absence of antegrade or retrograde ejaculation and is often linked to neurological dysfunction or drugs. Painful ejaculation, though poorly understood, is associated with infections, inflammation, malignancies, and psychological factors. Retrograde ejaculation results from failure of bladder neck closure during ejaculation and can be caused by neurogenic, pharmacological, or anatomical factors. Anorgasmia is primarily psychological in origin and often coexists with other ejaculatory disorders. Haemospermia, the presence of blood in ejaculate, is usually benign but warrants thorough evaluation to exclude malignancy or infection [Ref. 5.4: 0FLXCK].
Risk minimisation measures	Sexual dysfunction (decreased libido, erectile dysfunction and ejaculation disorders) has been addressed in SmPC Section 4.8 4.

Table II.B.1.2: Important Identified Risk: Sexual Dysfunction (Decreased Libido, Erectile Dysfunction and Ejaculation Disorders).

	Additional risk minimisation measures: A patient card will be provided inside the medication box for each patient. The risk is addressed as impaired sexual function through this patient card, which offers clear information to patients on recognizing symptoms and seeking timely medical advice. The risk is addressed through the Direct Healthcare Professional Communication (DHPC), which delivers targeted guidance to prescribers and other healthcare professionals to ensure appropriate monitoring and management.

Table II.B.1.3: Important Identified Risk: Depressive Disorders

Evidence for linking the risk to the medicine	Although a causal relationship with PROPECIA has not been established between PROPECIA and depressive disorders, depressive disorders may have a meaningful impact on the individual patient.
Risk factors and risk groups	Multiple risk factors have been reported to be associated with depression in men. Some of the risk factors are as follows: socioeconomic status such as unemployment/financial strain, not having children/having more children and low educational attainment; personal or family history of depression; alcohol or substance abuse; major life changes; trauma (including mental trauma such as childhood abuse, loneliness, death of spouse, divorce); stress and certain physical illnesses such as vascular brain changes, cancer, diabetes, and malnutrition and medications. Several emotional states and traits, such as neuroticism negative self-concept (with self-perceptions of worthlessness and uselessness), and negative interpretation or attention biases have also been linked to depression [Ref. 5.4: 0FLX7D], [Ref. 5.4: 0FLXBJ], [Ref. 5.4: 0FLXBL].
Risk minimisation measures	Routine risk minimisation measures:

Table II.B.1.3: Important Identified Risk: Depressive Disorders

	SmPC Section 4.4 (Mood alterations and depression) recommends monitoring patients for psychiatric symptoms. Depression is addressed in SmPC Section 4.8 Undesirable effects.

Table II.B.2.1: Important Identified Risk: Suicidal ideation

Risk minimisation measures	Routine risk minimisation measures : SmPC Section 4.4 (Suicidal ideation) recommends monitoring patients for psychiatric symptoms. Suicidal ideation is addressed in SmPC Section 4.8 Undesirable effects. Additional risk minimisation measures: A patient card will be provided inside the medication box for each patient. The risk is addressed as suicidal thoughts through this patient card, which offers clear information to patients on recognizing symptoms and seeking timely medical advice. The risk is addressed through the Direct Healthcare Professional Communication (DHPC), which delivers targeted guidance to prescribers and other healthcare professionals to ensure appropriate monitoring and management.

Table II.B.2.2: Important Identified Risk: Sexual Dysfunction (Decreased libido, Erectile Dysfunction and Ejaculation Disorders).

Risk minimisation measures	Sexual dysfunction (decreased libido, erectile dysfunction and ejaculation disorders) has been addressed in SmPC Section 4.8 Additional risk minimisation measures: A patient card will be provided inside the medication box for each patient. The risk is addressed as impaired sexual function through this patient card, which offers clear information to patients on recognizing symptoms and seeking timely medical advice. The risk is addressed through the Direct Healthcare Professional Communication (DHPC), which delivers

Table II.B.2.2: Important Identified Risk: Sexual Dysfunction (Decreased libido, Erectile Dysfunction and Ejaculation Disorders).

	targeted guidance to prescribers and other healthcare professionals to ensure appropriate monitoring and management.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of finasteride 0.2 and 1 mg.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for finasteride 0.2 and 1 mg.