VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Male hypogonadism is a condition in which the body does not produce enough testosterone. Testosterone is made naturally in your body in your testicles. It helps produce sperm and to develop and maintain the male sexual characteristics such as deep voice and body hair. It is also necessary for normal sexual function and sex drive. Testosterone also helps to maintain muscle size and strength.

There is a high prevalence of hypogonadism in the older adult male population. Hypogonadism increases with age and is significantly associated with obesity, type 2 diabetes, hypertension, osteoporosis and metabolic syndrome. Prevalence is low in men less than 70 years of age (3.1-7.0%) and increased to 18.4% in males above 70 years of age. No differences are seen between ethnic groups. The main symptoms of hypogonadism are reduced libido, erectile dysfunction, reduced muscle mass and strength, increased adiposity, low bone mass, depressed mood and fatigue.

VI.2.2 Summary of treatment benefits

Based on the available data from clinical studies and clinical experience of several years it is shown that testosterone, such as TESTAVAN, represents an effective drug in the treatment of male hypogonadism.

If administered as indicated in the Summary of Product Characteristics and taking into account the contraindications, the warnings and precautions, TESTAVAN can be considered effective in the approved indications.

VI.2.3 Unknowns relating to treatment benefits

No gaps in knowledge about efficacy in the target population have been identified.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Risk of transfer of testosterone to other persons (secondary exposure)	If no precaution is taken, testosterone gel can be transferred to other persons by close skin to skin contact. If the contact is repeated or prolonged, this may cause, unwanted side effects such as growth of facial and/or body hair, acne, deepening of the voice or changes in the menstrual cycles of women). Similarly, children have naturally low concentrations of testosterone and could be harmed by higher levels.	It is important that you do not spread the medicine to others, especially women and children. To stop the gel being transferred from your skin to someone else, the following precautions are recommended: • use the cap applicator for hands-free administration to reduce the risk of secondary exposure to testosterone • wash your hands with water and soap immediately if you accidently get any Testavan on your hands • cover the application site with clothing once the gel has dried • have a bath or shower, or wear clothing to cover the gel application site (e.g. a T-shirt), before having close skin-to-skin contact with anyone • leave a long period of time between putting on the gel and having sex or other close skin to skin contact with anyone. Pregnant women must avoid all contact with Testavan. If your partner is pregnant you must be careful and protect her from any contact with Testavan. If someone else is exposed to Testavan either as a result of contact with the gel itself or because of contact with the application area on your skin, the person should wash their area of skin contact with soap and water

Risk	What is known	Preventability
		as soon as possible. The longer that the gel is in contact with the skin before washing, the greater the chance that the person will absorb some testosterone. This is particularly important for women, especially pregnant or breast-feeding women, and children. If they develop signs such as acne or changes in the growth or pattern of hair on their face or body, they should see their doctor.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Prostate cancer	Testosterone treatment may accelerate the progression of pre-existing prostate cancer. Your doctor will perform the necessary tests before starting treatment and then check by carrying out periodic blood tests and prostate examinations. Talk to your doctor or pharmacist before using TESTAVAN, if you have difficulty in passing water (urinating), which may be due to an enlarged prostate gland.
Condition that affects the supply of blood to the heart (cardiovascular risks)	No clear understanding of the mechanism could be identified in the scientific literature. Talk to your doctor or pharmacist before using TESTAVAN, if you have ischaemic heart disease (which affects the supply of blood to the heart).

Missing information

Risk	What is known
Limited information on use in patients with heart, kidney, and liver diseases.	These patients have not been studied, as there is a known class effect of testosterone in these groups of patients. In patients suffering from severe heart, liver or kidney disease, treatment with TESTAVAN may cause severe complications in the form of water retention in your body sometimes accompanied by (congestive) heart failure.
Safety in elderly males ≥65 years of age	There is limited experience on the safety and efficacy of the use of TESTAVAN in patients over 65 years of age. Currently, there is no consensus concerning age specific reference values for testosterone. However it should be taken into consideration that the physiologically testosterone serum levels are lower with increasing age.[1]

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.

This medicine has no additional risk minimisation measures

The Summary of Product Characteristics and the Package leaflet for TESTAVAN can be found via the webpage of the national medicinal agencies.

VI.2.6 Planned post authorisation development plan

Not applicable (no planned post authorisation studies).

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

Table 1: Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	15 December 2016	Identified Risks • Hypertension worsened • Haematocrit increased • Secondary exposure Potential Risks • Prostate cancer • Ischemic heart disease Missing information • Cardiac, renal and hepatic failure patients have not been studied as there is a known class effect of testosterone in these populations • Safety in elderly males ≥65 years of age	No comments
2.0	20 September 2017	Identified Risks • Secondary exposure Potential Risks • Prostate cancer • Cardiovascular risks • Oedema with or without congestive cardiac failure	List of identified risks, potential risks and missing information updated according to comments received from the Reference Member State during the European approval

Version	Date	Safety Concerns	Comment
		in patients suffering from severe cardiac, hepatic or renal insufficiency Missing information • Safety in elderly males ≥65 years of age	process.

References

[1] EU Pharmacovigilance Risk Assessment Committee (PRAC) Assessment report; 09 October 2014; EMA/716062/2014.