Summary of risk management plan for Testosterone Logenex 1000mg/4ml, solution for injection (testosterone undecanoate)

This is a summary of the risk management plan (RMP) for Testosterone Logenex (testosterone undecanoate). The RMP details important risks of Testosterone Logenex, how these risks can be minimised, and how more information will be obtained about Testosterone Logenex risks and uncertainties (missing information). Important new concerns or changes to the current ones will be included in updates of Testosterone Logenex's RMP.

Testosterone Logenex's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Testosterone Logenex should be used.

Important new concerns or changes to the current ones will be included in updates of this RMP for testosterone undecanoate.

I. The medicine and what it is used for

Testosterone Logenex is authorised for testosterone replacement therapy for male hypogonadism (see SmPC for the full indication). It contains testosterone undecanoate as the active substance and it is given by intramuscular injection.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Testosterone Logenex together with measures to minimise such risks and the proposed studies for learning more about testosterone undecanoate's risks, are outlined below.

Measures to minimise 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 minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In the case of Testosterone Logenex, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.
In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (PSUR) assessment, so 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 Testosterone Logenex are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Testosterone Logenex. 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).

List of important risks and missing information	
Important identified risks	Pulmonary oil microembolism (POME)

Important potential risks	Thromboembolic risk secondary to haematocrit increase
Missing information	None

II.B Summary of important risks

Important identified risk: Pulmonary oil microembolism (POME)	
Evidence for linking the risk to the product	Testosterone Logenex is formulated to contain 1,000 mg of testosterone undecanoate in a 4 ml oily solution. Pulmonary microembolism of oily solutions can lead to signs and symptoms such as cough, dyspnoea, malaise, hyperhidrosis, chest pain, dizziness, paraesthesia, or syncope. These signs and symptoms may occur during or immediately after the injection and are typically benign and transient. Cases suspected to represent oily pulmonary microembolism have been reported rarely in clinical trials (in ≥1/10,000 and <1/1,000 injections) as well as from post-marketing data published in the literature. POME is classified as an important identified risk, due to the recognised causal relationship with oily solutions injection procedure, requiring risk minimisation measures to reduce its occurrence and consequently reduce the impact on the benefit-risk balance of the product. Such measures include specific clinical actions recommended in the SmPC and additional educational brochure for health care professionals
	on the correct injection technique, recognition and management of POME.
Risk factors and risk groups	Patients inadvertently injected intravascularly or too rapidly can be hypothesised to be at increased risk.

Risk minimisation measures	Routine risk minimisation measures: Routine risk communication: • SmPC sections 4.2, 4.4 and 4.8. Routine risk communication recommending specific clinical measure to address the risk: • Recommendations to monitor for symptoms during and immediately after each injection (to allow early recognition) and information on supportive treatment (e.g. by administration of supplemental oxygen) are provided in SmPC sections 4.4 and 4.8. Other routine risk minimisation measures beyond the Product Information: • This is prescription only medicine for use as directed by medical practitioner. Additional risk minimisation measures: Educational brochure for health care professionals on the correct injection technique, recognition and management of POME.
Additional pharmacovigilance activities	None.

Important potential risk: Thromboembolic risk secondary to haematocrit increase	
Evidence for linking the risk to the product	Polycythaemia, haematocrit increased, red blood cell count increased, and haemoglobin increased have been reported commonly in clinical trials (in ≥1/100 and <1/10 patients). Cardiovascular disorder has been reported uncommonly (in ≥1/1,000 and <1/100 patients). Recommendations for monitoring of haemoglobin and haematocrit in patients receiving long-term androgen therapy are provided in the SmPC.
	As the thromboembolic risk secondary to haematocrit increase requires routine risk minimisation recommendations for special clinical actions to reduce its impact on the benefit-risk balance, and because activities to further assess its relatedness and impact are being carried out, it is regarded as important potential risk.

Risk factors and risk groups	Stimulation of erythropoiesis is an expected pharmacodynamic effect of any testosterone replacement therapy [1]. Excessive increases in haematocrit and correspondingly increase of thromboembolism conceivable only with supraphysiological testosterone levels. Patients with additional risk factors for polycythaemia (e.g. chronic obstructive pulmonary disease), venous or arterial thromboembolism may be assumed to be at higher risk. Elderly patients might be at increased risk for the development of increased haematocrit under testosterone treatment [2,3].
Risk minimisation measures	Routine risk minimisation measures: Routine risk communication: • SmPC sections 4.4 and 4.8. Routine risk communication recommending specific clinical measure to address the risk: • Recommendations on monitoring haemoglobin and haematocrit (SmPC section 4.4). Other routine risk minimisation measures beyond the Product Information: • This is prescription only medicine for use as directed by medical practitioner.
Additional pharmacovigilance activities	None.

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 Testosterone Logenex.

II.C.2 Other studies in post-authorisation development plan

There are no other studies required for Testosterone Logenex.

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