PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR SENSTEND (LIDOCAINE / PRILOCAINE)

This is a summary of the risk management plan (RMP) for Senstend cutaneous spray, solution (150 mg/ml lidocaine / 50 mg/ml prilocaine). The RMP details important risks of Senstend, how these risks can be minimised, and how more information will be obtained about Senstend's risks and uncertainties (missing information).

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

This summary of the RMP for Senstend should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones are included in updates of Senstend's RMP.

I. The medicine and what it is used for

Senstend is authorised for the treatment of the signs and symptoms of premature ejaculation (see SmPC for the full indication). It contains lidocaine and prilocaine as the active substances and it is given topically as a cutaneousspray. A single dose of Senstend (3 actuations) consists of a total of 22.5 mg lidocaine and 7.5 mg prilocaine.

Further information about the evaluation of Senstend's benefits can be found in Senstend's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/senstend.

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

Important risks of Senstend, together with measures to minimise such risks and the proposed studies for learning more about Senstend 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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Senstend is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Senstend 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 Senstend. 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 longterm use of the medicine).

Table VI-1 Summary table of important risks and missing information

Important identified risks	Erectile dysfunction
Important potential risks	Hypersensitivity Carcinogenicity at the application site Systemic exposure leading to systemic reactions (e.g. methaemoglobinaemia, systemic malignancies) Inadvertent trauma secondary to hypoaesthesia (including application to unintended sites including eyes, oral cavity and anus) Partner exposure (leading to application site reactions, hypersensitivity reactions, trauma secondary to hypoaesthesia) Effect on fertility Interference with contraception
Important missing information	Use in men whose sexual partner may be pregnant Long term clinical safety Patients older than 65 years

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Important identified risk: Erectile Dysfunction	
Evidence for linking the risk to the medicine	Theoretically the local anaesthetic effect of Senstend could affect nerve endings in the penis and aggravate ED. The overall incidence of erectile dysfunction in the clinical trial programme for Senstend was 4.4%. None of the reports of erectile dysfunction were classified as "serious adverse reactions". Outcome data was not collected for all reports; however reports of severe ED (see below), resolved without treatment. If the patient suffers ED on treatment with Senstend (or their co-existing ED is aggravated), they have the option of discontinuing Senstend, and any effect of the Senstend should be short-lived, based on the duration of action of lidocaine and prilocaine.
Risk factors and risk groups	Not determined.
Risk minimisation measures	Routine risk communication • SmPC section 4.8. • PL section 4. Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 4.4. • PL section 2.

Important identified risk: Hypersensitivity	
Evidence for linking the risk to the medicine	Hypersensitivity reactions are a Type I immune response. Type 1 hypersensitivity reactions can be life-threatening and may, therefore, require immediate treatment and hospitalisation. If the incidence of reporting indicates that these reactions are no longer only "very rare" (<1/10,000), type 1 hypersensitivity reactions would be a potential public health impact of safety concern.
Risk factors and risk groups	All patients who are hypersensitive to agents of any kind, particularly to amide local anaesthetics.
Risk minimisation measures	Routine risk communication • SmPC section 2. • SmPC section 6.1. • PL section 4. Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 4.3. • SmPC section 4.4. • PL section 2.

Important identified risk: Carcinogenicity at the application site	
Evidence for linking the risk to the medicine	Local metabolism of prilocaine and lidocaine to *o*-toluidine and 2, 6-xylidine, which have carcinogenic potential. As for every case of penile cancer, the impact on patients will depend on stage detected and response to treatment.
Risk factors and risk groups	Not identified to date.
Risk minimisation measures	Routine risk communication • SmPC section 5.3.

Important identified risk: Systemic exposure leading to systemic reactions (e.g. methaemoglobinaemia, systemic malignancies)	
Evidence for linking the risk to the medicine	Methaemoglobinaemia: Oxidation of critical level of haemoglobin to the ferric state (Fe3+) by the drug substances. Methaemoglobinaemia can be prevented by ensuring that Senstend is not concomitantly administered with other drugs that can also induce methaemoglobinaemia, or administered to susceptible individuals (due to concomitant medical conditions) or whose sexual partner is susceptible, as are listed in the Product Information. Methaemoglobinaemia is dose dependent. Due to the low dose of Senstend applied, the level of methaemoglobinaemia is also likely to be low.
Risk factors and risk groups	Methaemoglobinaemia: Those with pre-existing methaemoglobinaemia or those being concomitantly administered with other drugs that can also cause the condition. Systemic malignancies: No data collected to date.
Risk minimisation measures	Routine risk communication • SmPC section 4.8. • PL section 4. Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 4.2. • SmPC section 4.4. • SmPC section 4.5. • SmPC section 4.9. • PL section 2.

Important identified risk: Inadvertent trauma secondary to hypoaesthesia (including application to unintended sites including eyes, oral cavity and anus)	
Evidence for linking the risk to the medicine	Hypoaesthesia, which can lead to inadvertent trauma, is caused by the local anaesthetic effects of the drug substances. This hypoaesthesia may mask normal pain sensations and, therefore, increases the dangers of localised injury. In clinical trials, all male patients and female partners recovered from hypoaesthesia without treatment. There were no recorded cases of trauma occurring as a result of genital (or other area) hypoaesthesia in the clinical trials.
Risk factors and risk groups	All patients who suffer hypoaesthesia or apply the medicinal product to unintended sites are at risk.
Risk minimisation measures	Routine risk communication • SmPC section 4.8. • PL section 4. Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 4.4. • PL section 2.

Important identified risk: Partner exposure (leading to application site reactions, hypersensitivity reactions, trauma secondary to hypoaesthesia)	
Evidence for linking the risk to the medicine	Hypersensitivity or other application site reactions will be caused by an immune response. All partners are at risk of hypersensitivity or application site reactions. Senstend is contraindicated in patients, or their partners, with hypersensitivity to any of the ingredients in Senstend or to local anaesthetics of the amide type. Only one report of vulvovaginal burning was considered severe in nature. In clinical trials, all female partners recovered from the above reactions without treatment.
Risk factors and risk groups	All partners are at risk of hypersensitivity or application site reactions. Senstend is contraindicated in patients, or their partners, with hypersensitivity to any of the ingredients in Senstend or to local anaesthetics of the amide type.
Risk minimisation measures	Routine risk communication • SmPC section 2. • SmPC section 4.8. • SmPC section 6.1. • PL section 4. Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 4.3. • SmPC section 4.4. • PL section 2.

Important identified risk: Effect on fertility	
Evidence for linking the risk to the medicine	Lidocaine and Prilocaine impede nerve conductivity by interfering with sodium ion channel function in cell membranes. Hence sperm motility could be affected. Patients hoping to achieve conception are advised to either avoid using Senstend, or - if Senstend is essential to achieve penetration – are advised to wash the glans penis thoroughly 5 minutes after applying Senstend, but prior to intercourse.
Risk factors and risk groups	Patients who require use of Senstend to achieve penetration are at risk. No effect on humans reported to date. An ex-vivo study (Study Number 495000) to assess the effect of Senstend on rat sperm motility showed that Senstend did have a negative effect, but at concentrations many fold greater than those the sperm would be exposed to in clinical use.
Risk minimisation measures	Routine risk communication • SmPC section 4.8. • SmPC section 5.3. • PL section 4. Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 4.4. • SmPC section 4.6. • PL section 2.

Important identified risk: Interference with contraception	
Evidence for linking the risk to the medicine	Interaction of Senstend with polyurethane causing decrease in its tensile strength. Patients are informed not to use polyurethane-based barrier contraceptives with Senstend.
Risk factors and risk groups	Patients or partners using polyurethane-based female or male condoms. Device interaction testing conducted with barrier contraceptives showed that the tensile strength of polyurethane devices (female and male condoms) was compromised, causing increased puncture rates. Devices made from latex rubber, polyisoprene, nitrile and silicone were unaffected. 1. Outcome will be unplanned pregnancy. 2. If the device suffers significant damage, it could increase the risk of sexually transmitted diseases.
Risk minimisation measures	Routine risk communication • SmPC section 4.4. Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 6.2. • PL section 2.

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 obligations of Senstend.

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

There are no studies required for Senstend.