SUMMARY OF RISK MANAGEMENT PLAN FOR PRILIGY (DAPOXETINE)

This is a summary of the risk management plan (RMP) for Priligy. The RMP details important risks of Priligy, how these risks can be minimised, and how more information will be obtained about Priligy's risks and uncertainties (missing information).

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

I. THE MEDICINE AND WHAT IT IS USED FOR

Priligy is authorised for the treatment of premature ejaculation (PE) in adult men aged 18 to 64 years (see SmPC for the full indication). It contains dapoxetine as the active substance and it is given by oral route of administration [30 or 60 mg film-coated tablets].

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Priligy, together with measures to minimise such risks and the proposed studies for learning more about Priligy'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 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.*

II.A. List of important risks and missing information

Important risks of Priligy are risks that need special risk management activities to further investigate or minimise 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 Priligy. 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	Syncope
Important potential risks	None
Missing information	None

II.B. Summary of important risks

Important identified risk: Syncope	
Evidence for linking the risk to the medicine	In a population-based study (the sample consisted almost entirely of middle-aged and older white men and women), the incidence of syncope was similar between men and women, but was not constant across age groups, increasing more rapidly starting at the age of 70 years. Vasovagal syncope cases represented 24% of the total events, resulting in an incidence of 1.31 per 1,000 person-years (although the difference between sexes was not described).
Risk factors and risk groups	There are several factors associated with syncope following dosing with dapoxetine such as location of the subject at the time of the event, first versus subsequent exposure to the drug, temporal relationship to dosing, and dose level (30 mg versus 60 mg), observed during clinical studies. *Onsite versus offsite dosing* During clinical development, the majority of cases occurred in a controlled setting at the site (onsite) versus in the home environment (offsite) despite that the majority of dapoxetine doses were taken offsite (e.g., at home). Various procedures, such as vital sign measurements, orthostatic manoeuvres, ECG/Holter recordings, and venipunctures may have contributed to the higher onsite incidence of syncope, as these and similar factors are known to contribute to or trigger vasovagal syncope. *Factors contributing to offsite syncope occurrence* There are several well-recognized risk factors that contribute to the syncopal events that occurred offsite including attaining or remaining in a standing position, pain, fear, emotional stress, or the anticipation of pain or trauma, instrumentation, defaecation, micturition, or cough, and circumstances that can result in a decrease of cardiac performance (i.e., dehydration, potentially due to physical activity in a warm environment, or alcohol or recreational drugs and other medications that may reduce orthostatic intolerance when manoeuvering from a sitting to a standing position). *First versus subsequent dose* Considering the data collected in clinical trials, the number of subjects reporting a syncopal event with the first dose of dapoxetine is higher than number of subjects reporting a syncopal event with a subsequent dose of the drug. These data remain valid when dapoxetine is administered onsite; however, in the offsite administration (e.g., at home), the percentage of subjects with a case of syncope associated with the first dose of dapoxetine is similar to the incidence observed for subsequent doses. *Apparent temporal relationship to pharmacokinetics* The temporal relationship between syncope and dosing indicates that the majority of the cases identified during clinical development trials, occurred during the first 3 hours after dosing with dapoxetine, when the blood concentration of the drug would be expected to be the highest. *Reported presyncopal symptoms*

	Considering the data collected in clinical trials, although not all subjects experiencing a syncopal event presented presyncopal symptoms, the most reported prodromal symptoms were nausea and dizziness. *Dose level* The incidence of syncope observed during clinical trial development was higher with the 60-mg dose level than the incidence observed with the 30-mg dose level. Based on this, a relationship between the incidence of syncope and dapoxetine dosing is suggested. *Other known risk factors for syncope* Other known risk factors that may contribute to the occurrence of syncope independent of dapoxetine usage include: • Certain heart conditions, (i.e., blood flow obstructions and arrhythmias); • Heart failure (NYHA class II-IV) • Conduction abnormalities (second- or third-degree AV block or sick sinus syndrome) not treated with a permanent pacemaker • Significant ischaemic heart disease • Significant valvular disease • Illnesses that affect the autonomic nervous system, such as Parkinson's disease; • Anxiety or panic disorders; • Diabetes; • Alcohol use; • Dehydration; • Certain prescription medications, (i.e., some antihypertensive medicines that lower BP); • Low blood sugar; • Lean body mass; and • Previous history of vasovagal syncope.
Risk minimisation measures	Routine risk minimisation measures: - SmPC section 4.3 Contraindications - SmPC section 4.4 Special warnings and precautions for use - SmPC section 4.5 Interaction with other medicinal products and other forms of interaction - SmPC section 4.7 Effects on ability to drive and use machines - SmPC section 4.8 Undesirable effects - PL section 2 What you need to know before you take dapoxetine Do not take dapoxetine Warnings and precautions Dapoxetine with food, drink and alcohol Driving and using machines PL section 4 Possible side effects Legal status: prescription only medicine Additional risk minimisation measures: No risk minimisation measures

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 Priligy.

II.C.2. Other studies in post-authorisation development plan
There are no studies required for Priligy.