SUMMARY OF RISK MANAGEMENT PLAN FOR SUNOSI (SOLRIAMFETOL)

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

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

This summary of the RMP for Sunosi 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 will be included in updates of Sunosi's RMP.

I THE MEDICINE AND WHAT IT IS USED FOR

Sunosi is authorised for improving wakefulness and reducing excessive daytime sleepiness in adult patients with narcolepsy (with or without cataplexy) or obstructive sleep apnoea whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP) (see SmPC for the full indication). It contains solriamfetol as the active substance and it is given orally.

Further information about the evaluation of Sunosi's benefits can be found in Sunosi'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/sunosi >.

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

Important risks of Sunosi, together with measures to minimise such risks and the proposed studies for learning more about Sunosi'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 authorized 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 (eg, 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 Periodic Safety Update Report (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 Sunosi is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Sunosi 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 Sunosi. 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 (eg, on the long-term use of the medicine).

List of Important Risks and Missing Information	
Important identified risks	Serious cardiovascular events
Important potential risks	Serious psychiatric events Potential for abuse, misuse and diversion Reproductive toxicity
Missing information	Potential for pharmacodynamic interactions Use in lactating women

II.B Summary of Important Risks

Important Identified Risk: Serious Cardiovascular (CV) Events	
Evidence for linking the risk to the medicine	The general patient population with narcolepsy or OSA may be at risk for serious CV events due to certain intrinsic factors such as age, obesity, and comorbid cardiovascular and metabolic conditions, as well as underlying disease pathophysiology. CV adverse events were of interest because of observations of modest, reversible increases in HR and BP.
Risk factors and risk groups	Patients with narcolepsy and OSA may be at risk for CV events due to certain intrinsic risk factors, such as increasing age, obesity, concurrent diabetes mellitus, concurrent CV disease, and smoking. Patients with pre-existing hypertension, cardiovascular or cerebrovascular conditions that might be compromised by increases in blood pressure.

	Other risk groups include patients using concomitant medications that increase heart rate and blood pressure.
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.2, 4.3, 4.4 and 4.8 and corresponding PIL sections Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Long-term safety PASS for OSA patients. See section II. C of this summary for an overview of the post-authorisation development plan.

Important Potential Risk: Serious Psychiatric Events	
Evidence for linking the risk to the medicine	Psychiatric adverse events were of interest because psychiatric comorbidities are common in narcolepsy and OSA, and stimulants and wake-promoting agents have the potential to exacerbate underlying psychiatric conditions.
Risk factors and risk groups	Psychiatric disorders are a frequent comorbidity in patients with narcolepsy. In OSA patients, observational studies have found a nearly 2-fold higher incidence of depression in patients with OSA when matched to controls without OSA. In the Sunosi clinical development programme, serious psychiatric symptoms occurred more commonly in the narcolepsy population than the OSA population.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8 and corresponding PIL sections Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Long-term safety PASS for OSA patients. See section II. C of this summary for an overview of the post-authorisation development plan.

Important Potential Risk: Potential for Abuse, Misuse and Diversion	
Evidence for linking the risk to the medicine	Sunosi meets the criteria for assessment of abuse potential as a new molecular entity that affects the CNS. In addition, abuse, misuse and diversion potential are associated with other medications used in the treatment of ES that are pharmacologically similar to Sunosi.
Risk factors and risk groups	Patients with a history of substance abuse (alcohol and /or drugs)
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and corresponding PIL sections Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Long-term safety PASS for OSA patients See section II. C of this summary for an overview of the post-authorisation development plan.

Important Potential Risk: Reproductive Toxicity	
Evidence for linking the risk to the medicine	Preclinical reproductive toxicity studies in pregnant rats and rabbits showed evidence of embryofoetal toxicity.
Risk factors and risk groups	Pregnant women and their offspring.
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4, 4.6 and 5.3 and corresponding PIL sections Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Two post-marketing pregnancy registries See section II. C of this summary for an overview of the post-authorisation development plan.

Missing Information: Potential for Pharmacodynamics Interactions	
Risk minimization measures	Routine risk minimisation measures: SmPC section 4.2, 4.3 and 4.5 and corresponding PIL sections Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Long-term safety PASS for OSA patients. See section II. C of this summary for an overview of the post-authorisation development plan.

Missing Information: Use in Lactating Women	
Risk minimization measures	Routine risk minimisation measures: SmPC section 4.6 and corresponding PIL sections Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Post-marketing lactation study See section II. C of this summary for an overview of the post-authorisation development plan.

II.C Post-Authorisation Development Plan

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

There are no studies that are conditions of the marketing authorisation or specific obligation of Sunosi.

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

A prospective, non-interventional, post-authorisation safety study to evaluate the long term safety of solriamfetol in adult patients with obstructive sleep apnoea (OSA) treated with solriamfetol according to an agreed protocol.

Purpose of the study: The primary objective of the PASS will assess the risk of CV events among patients with OSA newly initiating treatment with Sunosi (solriamfetol) compared to Sunosi-unexposed patients with OSA, with or without other pharmacologic treatments to

improve wakefulness, in real-world practice. Secondary objectives include collection and analysis of data on psychiatric events, a sensitivity analysis on the primary objective for patients receiving supratherapeutic doses to explore the influence of possible aberrant drug-related behaviours (abuse, misuse and diversion), and assessment of possible PD interactions by collection of data on concomitant medications as part of the primary objective and analysis of events of interest.

Sunosi (solriamfetol) Pregnancy Registry: an observational study on the safety of solriamfetol exposure in pregnant women and their offspring

Purpose of the study: The objective of the Sunosi (solriamfetol) Pregnancy Registry is to compare the maternal, fetal, and infant outcomes of women exposed to solriamfetol during pregnancy with outcomes in an unexposed comparator population.

A retrospective database study to assess pregnancy outcomes associated with use of solriamfetol

Purpose of the study: The goal of this project is to use existing data sources to evaluate pregnancy and infant outcomes.

A Phase 4, Open-Label, Single-Dose Study to Evaluate Sunosi (solriamfetol) Pharmacokinetics in Breast Milk of Healthy Postpartum Women Following Oral Administration of Sunosi

Purpose of the study: Primary objectives: 1) Evaluate solriamfetol pharmacokinetics (PK) in breast milk; 2) Estimate the daily solriamfetol dose received by the infant from the breast milk of the nursing mother. Secondary objective: Assess the safety and tolerability of single oral doses of solriamfetol in healthy postpartum women.