PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Lisdexamfetamine 'Aspire' kapsler hårde 20/30/40/50/60/70 mg, Lisdexamfetamine Aspire 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg kapselit, kovat, Lisdexamfetamine Aspire 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg Hartkapseln and Lisdexamfetamine Aspire 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg harde capsules and Lisdexanfetamina 20/30/40/50/60/70 mg cápsulas, duras and Lisdexamfetamine Aspire 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg Kapsel, hard and Lisdexamfetamine Aspire (herein referred to as Lisdexamfetamine):

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

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

I. The medicine and what it is used for

Lisdexamfetamine is authorised:

- as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged 6 years and over when response to previous methylphenidate treatment is considered clinically inadequate.
- as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in adults with pre-existing symptoms of ADHD in childhood.

It contains Lisdexamfetamine dimesylate as the active substance and it is given by oral route.

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

Important risks of Lisdexamfetamine, together with measures to minimise such risks and the proposed studies for learning more about Lisdexamfetamine'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 PL and SmPC addressed to patients and health care 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, 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 Lisdexamfetamine 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 Lisdexamfetamine. 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	• Intentional drug misuse, abuse and diversion • Growth retardation and developmental delay in children and adolescents • Psychosis/Mania • Hostility/Aggression • Depression
Important potential risks	• Serious cardiovascular events (including arrhythmias, ischaemic cardiac events, cardiomyopathy, sudden death) • Cerebrovascular disorders (ischaemic and haemorrhagic stroke) • Syncope • Suicidality • Off-label use • Neonatal effects on growth (via lactation)
Missing information	• Safety in pregnant women • Safety in the elderly • Long-term safety (cardiovascular and cerebrovascular effects) in adults

II.B Summary of important risks

<u>Important identified risks</u>

Intentional drug misuse, abuse and diversion	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.1, 4.2, 4.4 and 5.1 • PL section 2 SmPC section 4.2: Patients should be monitored for the risk of diversion, misuse, and abuse.

	SmPC section 4.4: Stimulants should be prescribed cautiously to patients with a history of substance abuse or dependence. **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment • Potential for non-medical use & diversion of prescription stimulant medications Leaflet

Growth retardation and developmental delay in children and adolescents	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.2, 4.4, 4.6 and 4.8 • PL sections 2 and 4 SmPC section 4.4 includes recommendation to monitor growth during treatment **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment

Psychosis/Mania	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.4 and 4.8 • PL section 4 SmPC section 4.4 includes recommendation to monitor growth during treatment SmPC section 4.4 includes recommendation to discontinue treatment in case possible causal role of the medicinal product in the emergence of manic symptoms **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate

	• Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment

Hostility/Aggression	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.2, 4.3, 4.4 and 4.8 • PL sections 2 and 4 **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment

Depression	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.2, 4.4 and 4.8 • PL sections 2 and 4 SmPC section 4.4 includes recommendation to screen for family history of depression prior to initiation of treatment **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment

Serious cardiovascular events (including arrhythmias, ischaemic cardiac events, cardiomyopathy, sudden death)	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.2, 4.3, 4.4, 4.8 and 4.9 • PL sections 2 and 4

	SmPC section 4.4 includes recommendation to screen for family history of sudden death or ventricular arrhythmia prior to initiation of treatment **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine lisdexamfetamine dimesylate treatment

Cerebrovascular disorders (ischaemic and haemorrhagic stroke)	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.2, 4.3, 4.4 and 4.8 • PL sections 2 and 4 SmPC section 4.4 includes recommendation not to treat patients with cardiac abnormalities with stimulants **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment

Suicidality	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC section 4.4 • PL section 2 SmPC section 4.4 includes recommendation to screen for family history of suicide prior to initiation of treatment **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment

	• Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment

Off-label use	
Risk minimisation measures	**Routine risk minimisation measures:** None **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment • Potential for non-medical use and diversion of prescription stimulant medications leaflet

Safety in pregnant women	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC section 4.6 • PL section 2 SmPC section 4.6 and PIL section 2 include warnings for use during pregnancy **Additional risk minimisation measures:** • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine dimesylate • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine dimesylate treatment • Chart for ongoing monitoring during lisdexamfetamine dimesylate treatment

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 Lisdexamfetamine.

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

There are no studies required for Lisdexamfetamine.