Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for Lisdexamfetamine Dimesylate 20 mg/30 mg/40 mg/50 mg/60 mg/70 mg hard capsules.

This is a summary of the risk management plan (RMP) for lisdexamfetamine dimesylate 20 mg/30 mg/40 mg/50 mg/60 mg/70 mg hard capsules (hereinafter referred to as lisdexamfetamine dimesylate). The RMP details important risks of lisdexamfetamine dimesylate, how these risks can be minimised, and how more information will be obtained about lisdexamfetamine dimesylate's risks and uncertainties (missing information).

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

Important new concerns or changes to the current ones will be included in updates of lisdexamfetamine dimesylate's RMP.

I. The Medicine and What It is used for.

Lisdexamfetamine dimesylate is authorised for indications as below:

Lisdexamfetamine dimesylate is indicated 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.

Lisdexamfetamine dimesylate is also indicated as part of a comprehensive treatment programme for ADHD in adults with pre-existing symptoms of ADHD in childhood.

Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders (for paediatric patients) or a specialist in behavioural disorders (for adult patients). Diagnosis should be based on a complete history and evaluation of the patient according to current Diagnostic and Statistical Manual of Mental Disorders criteria or International Classification of Diseases guidelines. Diagnosis cannot be made solely on the presence of one or more symptoms.

In adults, the presence of pre-existing symptoms of ADHD in childhood is required and should be confirmed retrospectively (according to the patient's medical record or, if not available, through appropriate and structured instruments or interviews). Based on clinical judgment, patients should have ADHD of at least moderate severity as indicated by at least moderate functional impairment in two or more settings (for example, social, academic, and/or occupational functioning), affecting several aspects of an individual's life.

The specific aetiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use of medical and specialised psychological, educational, and social resources.

Lisdexamfetamine dimesylate is not indicated in all patients with ADHD and the decision to use the medicinal product must take into consideration the profile of the patient, including a thorough assessment of the severity and chronicity of the patient's symptoms, the potential for abuse, misuse or diversion and clinical response to any previous pharmacotherapies for the treatment of ADHD.

A comprehensive treatment programme typically includes psychological, educational, behavioural, occupational and social measures as well as pharmacotherapy, as appropriate, and is aimed at stabilising the patient with a behavioural syndrome characterised by symptoms which may include chronic history of short attention span, distractibility, emotional lability, impulsivity, moderate to severe hyperactivity, minor neurological signs and abnormal electroencephalogram. Learning may or may not be impaired (for paediatric patients).

Appropriate educational placement is essential (for paediatric patients), and psychosocial intervention is generally necessary. The use of lisdexamfetamine dimesylate should always be used in this way according to the licensed indication.

It contains lisdexamfetamine dimesylate as the active substance and it is given orally as hard capsules (20 mg, 30 mg, 40 mg, 50 mg, 60 mg, and 70 mg).

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of lisdexamfetamine dimesylate, together with measures to minimise such risks and the proposed studies for learning more about lisdexamfetamine dimesylate's risks, if any, 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 lisdexamfetamine dimesylate, 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, 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 lisdexamfetamine dimesylate is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of lisdexamfetamine dimesylate are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered/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 dimesylate. 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).

Table 6 Summary of safety concerns

Summary of safety concerns	
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

Important identified risk: Intentional drug misuse, abuse, and diversion	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections: 4.1, 4.2 and 4.4 PL section: 2 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important identified risk: Growth retardation and developmental delay in children and adolescents	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections: 4.2, 4.4 and 4.8 PL sections: 2 and 4 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important identified risk: Psychosis/Mania	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections: 4.4, 4.8 PL section: 4 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important identified risk: Hostility/ Aggression	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections: 4.4, 4.8 and 4.9 PL sections: 2, 4 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important identified risk: Depression	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections: 4.4, 4.8 and 4.9 PL sections: 2, 4 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important potential risks: 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 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important potential risk: Cerebrovascular disorders (ischaemic and haemorrhagic stroke)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section: 4.3 PL section: 2 Legal status: Prescription only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important potential risk: Syncope	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC sections: 4.4 and 4.8 PL sections: 4 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** None

Important potential risk: Suicidality	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section: 4.4 PL section: 2 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important potential risk: Off-label use	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section: None PL sections: None Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Important potential risk: Neonatal effects on growth (via lactation)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section: 4.6

	PL section: 2 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** None

Missing Information: Safety in pregnant women	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section: 4.6 PL section: 2 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** A Physician's guide to prescribing with the following elements: • 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*.

Missing Information: Safety in the elderly	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section: 4.2 PL section: 3 Legal status: Prescription-only medicine. **Additional risk minimisation measures:** None.

Missing Information: Long-term safety (cardiovascular and cerebrovascular effects) in adults	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section: 4.2 PL section: 3

	Legal status: Prescription-only medicine. **Additional risk minimisation measures:** None.

* *The education materials (Checklist 1, Checklist 2, Chart and Leaflet) are different for patients below 18 years and for patients 18 years or above.*

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 dimesylate, hard capsules.

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

There are no studies required for lisdexamfetamine dimesylate, hard capsules.