13 Part VI: Summary of the risk management plan for Lisdexamfetamine diadipate, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg*, Hard capsules

*Strength expression corresponding to equivalent amount of innovator salt lisdexamfetamine dimesylate

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

Lisdexamfetamine diadipate, hard capsules' summary of product characteristics (SmPCs) and its package leaflets give essential information to healthcare professionals and patients on how lisdexamfetamine diadipate, hard capsules should be used.

Important new concerns or changes to the current ones will be included in updates of the lisdexamfetamine diadipate, hard capsules' RMP.

13.1 Part VI: I. The medicine and what it is used for

Lisdexamfetamine diadipate, hard capsules are authorized for:

30 mg, 50 mg and 70 mg, hard capsules (for adults)
Lisdexamfetamine diadipate is indicated as part of a comprehensive treatment program for attention deficit/hyperactivity disorder (ADHD) in adults.

Lisdexamfetamine diadipate is not indicated in all adult patients 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.

Treatment must be under the supervision of a specialist in behavioral disorders. Diagnosis should be based on a complete history and evaluation of the patient according to current Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria or International Classification of Diseases (ICD) guidelines. Diagnosis cannot be made solely on the presence of one or more symptom. In adults, the presence of symptoms of ADHD that were pre-existing 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 etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use of medical and specialized psychological, educational, and social resources.

A comprehensive treatment program typically includes psychological, educational, behavioral, occupational and social measures as well as pharmacotherapy and is aimed at stabilizing the adult patient with a behavioral syndrome characterized by symptoms which may include chronic history of short attention span, distractibility, impulsivity and hyperactivity.

20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg, hard capsules (for pediatrics)
Lisdexamfetamine diadipate is indicated as part of a comprehensive treatment program for ADHD in children aged 6 years and over when response to previous methylphenidate treatment is considered clinically inadequate.

Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioral disorders. Diagnosis should be made according to DSM criteria or the guidelines in ICD and should be based on a complete history and evaluation of the patient. Diagnosis cannot be made solely on the presence of one or more symptom.

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

A comprehensive treatment program typically includes psychological, educational and social measures as well as pharmacotherapy and is aimed at stabilizing children with a behavioral syndrome characterized 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 (EEG). Learning may or may not be impaired.

Lisdexamfetamine diadipate is not indicated in all children with ADHD and the decision to use the medicinal product must be based on a very thorough assessment of the severity and chronicity of the child's symptoms in relation to the child's age and potential for abuse, misuse or diversion.

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

It contains lisdexamfetamine diadipate as an active substance and is taken orally as hard capsules (20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg).

13.2 Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of lisdexamfetamine diadipate, hard capsules, together with measures to minimize such risks and the proposed studies for learning more about lisdexamfetamine diadipate, hard capsules' risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflets and SmPCs 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 (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute *routine risk minimization* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

In the case of lisdexamfetamine diadipate, hard capsules, these measures are supplemented with *additional risk minimization measures* mentioned under relevant important risks, below.

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

13.2.1 Part VI – II.A: List of important risks and missing information

Important risks of lisdexamfetamine diadipate, hard capsules are risks that need special risk management activities to further investigate or minimize 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 diadipate, hard capsules. 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 13-1 List of important risks and missing information

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, ischemic cardiac events, cardiomyopathy, sudden death)
	Cerebrovascular disorders (ischemic and hemorrhagic 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

13.2.2 Part VI – II.B: Summary of important risks

Table 13-2 Important identified risk: Intentional drug misuse, abuse and diversion

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.1, 4.2 and 4.4 PL section 3 Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-3 Important identified risk: Growth retardation and developmental delay in children and adolescents

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.2, 4.4, 4.6, 4.8 and 5.3 PL sections 3 and 4 Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-4 Important identified risk: Psychosis/Mania

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.2, 4.4 and 4.8 PL sections 2 and 4 Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements:

- Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate*
- Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment*
- Chart for ongoing monitoring during lisdexamfetamine diadipate treatment*
- Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-5 Important identified risk: Hostility/Aggression

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4 and 4.8 PL sections 2 and 4 Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-6 Important identified risk: Depression

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4, 4.8 and 4.9 PL sections 2, 3 and 4 Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-7 Important potential risk: Serious cardiovascular events (including arrhythmias, ischemic cardiac events, cardiomyopathy, sudden death)

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.2, 4.4, 4.8 and 4.9 PL sections 2, 3 and 4 Legal status: Prescription only **Additional risk minimization measures:**

	A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-8 Important potential risk: Cerebrovascular disorders (ischemic and hemorrhagic stroke)

Risk minimization measures	**Routine risk minimization measures:** SmPC section 4.4 Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-9 Important potential risk: Suicidality

Risk minimization measures	**Routine risk minimization measures:** None Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-10 Important potential risk: Off-label use

Risk minimization measures	**Routine risk minimization measures:** SmPC section 4.2 PL section 3 Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements:

	• Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

Table 13-10 Missing information: Safety in pregnant women

Risk minimization measures	**Routine risk minimization measures:** None Legal status: Prescription only **Additional risk minimization measures:** A Physician's guide to prescribing with the following elements: • Checklist 1: Prescriber checklist before prescribing lisdexamfetamine diadipate* • Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine diadipate treatment* • Chart for ongoing monitoring during lisdexamfetamine diadipate treatment* • Potential for non-medical use and diversion of prescription stimulant medications leaflet*

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

13.2.3 Part VI – II.C: Post-authorization development plan

13.2.3.1 II.C.1. Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of lisdexamfetamine diadipate, hard capsules.

13.2.3.2 II.C.2. Other studies in post-authorization development plan

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