Part VI: Summary of the risk management plan

Summary of risk management plan for Lupetodela, Nupirasgote and Vibetacone 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg hard capsules (lisdexamfetamine)

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

Lupetodela, Nupirasgote and Vibetacone 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg hard capsules' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Lupetodela, Nupirasgote and Vibetacone should be used.

I. The medicine and what it is used for

Lupetodela, Nupirasgote and Vibetacone 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg hard capsules are authorised as part of a comprehensive treatment programme for ADHD in children aged 6 years and over when response to previous methylphenidate treatment is considered clinically inadequate and as part of a comprehensive treatment programme for ADHD in adults with pre-existing symptoms of ADHD in childhood (see SmPC for the full indication). It contains lisdexamfetamine as the active substance, and it is given by oral administration.

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

Important risks of Lupetodela, Nupirasgote and Vibetacone, together with measures to minimise such risks and the proposed studies for learning more about Lupetodela, Nupirasgote and Vibetacone'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 so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

In the case of Lupetodela, Nupirasgote and Vibetacone, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

If important information that may affect the safe use of Lupetodela, Nupirasgote and Vibetacone is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Lupetodela, Nupirasgote and Vibetacone 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 Lupetodela, Nupirasgote and Vibetacone. 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

Important identified risk: Intentional drug misuse, abuse and diversion	
Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.1, 4.2 and 4.4 of the SmPC and Sections 2 and 3 of the PIL give warnings about the potential for abuse and misuse and the need for prescribers to consider the patient's medical history prior to prescribing the product and to monitor them throughout treatment. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment Leaflet for patient use

Important identified risk: Growth retardation and developmental delay in children and adolescents	
Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.2 and 4.4 of the SmPC and Section 2 of the PIL include guidance for patient height and weight to be taken pre-treatment and monitored throughout treatment, interrupting treatment who are not growing or gaining weight as expected. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment

Important identified risk: Psychosis/Mania	
Risk minimisation measures	**Routine risk minimisation measures:**

Important identified risk: Psychosis/Mania	
	Sections 4.4 and 4.8 of the SmPC and Sections 2 and 4 of the PIL. Section 4.4 of the SmPC provides guidance on discontinuation of treatment, should symptoms occur. Sections 2 and 4 of the PIL inform patients not to start taking the medicine if they feel unusually excited, over-active, or un-inhibited and to see a doctor if these symptoms develop during treatment. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment

Important identified risk: Hostility/Aggression	
Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.4 and 4.8 of the SmPC and Sections 2 and 4 of the PIL. Section 4.4 of the SmPC states that patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behaviour or hostility. Sections 2 and 4 of the PIL advises patients to talk to their doctor or pharmacist before starting treatment if they are feeling aggressive or unfriendly, or their aggression gets worse. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment

Important identified risk: Depression	
Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.4 and 4.8 of the SmPC and Sections 2 and 4 of the PIL.

Important identified risk: Depression	
	Section 4.4 of the SmPC states that patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder. Sections 2 and 4 of the PIL advise patients to talk to their doctor or pharmacist before starting treatment if they are feeling depressed. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment

Important potential risk: Serious cardiovascular events (including arrhythmias, ischaemic cardiac events, cardiomyopathy, sudden death)	
Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.2, 4.3, 4.4 and 4.8 of the SmPC and Sections 2, 3 and 4 of the PIL. Section 4.3 contraindicates use of lisdexamfetamine in patients with symptomatic cardiovascular disease, advanced arteriosclerosis and patients with moderate to severe hypertension. Sections 4.2 and 4.4 of the SmPC and Section 2 and 3 of the PIL include guidance on baseline assessment and ongoing monitoring via check-ups. Section 4.4 of the SmPC and Section 2 of the PIL provide additional information on patients in which treatment should be initiated with caution. Section 4 warns patients that if they get an uneven heartbeat or chest pain, breathlessness or swelling of the legs, they should see a doctor straight away. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment

Important potential risk: Serious cardiovascular events (including arrhythmias, ischaemic cardiac events, cardiomyopathy, sudden death)	
	Chart for ongoing monitoring during lisdexamfetamine treatment

Important potential risk: Cerebrovascular disorders (ischaemic and haemorrhagic stroke)	
Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.2, 4.3, 4.4 and 4.8 of the SmPC and Sections 2, 3 and 4 of the PIL. Section 4.3 contraindicates use of lisdexamfetamine in patients with symptomatic cardiovascular disease, advanced arteriosclerosis and patients with moderate to severe hypertension. Sections 4.2 and 4.4 of the SmPC and Sections 2 and 3 of the PIL include guidance on baseline assessment and ongoing monitoring via check-ups. Section 4.4 of the SmPC and Section 2 of the PIL provide additional information on patients in which treatment should be initiated with caution. Section 4 warns patients that if they get an uneven heartbeat or chest pain, breathlessness or swelling of the legs, they should see a doctor straight away. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment

Important potential risk: Suicidality	
Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.2 and 4.4 of the SmPC and Section 2 of the PIL include information on pre-treatment evaluation, including psychiatric disorders or symptoms. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine

Important potential risk: Suicidality	
	Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment

Important potential risk: Off-label use	
Risk minimisation measures	**Routine risk minimisation measures:** Section 4.2 of the SmPC and Section 2 of the PIL include information on off label groups. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment

Missing Information: Safety in pregnant women	
Risk minimisation measures	**Routine risk minimisation measures:** Section 4.6 of the SmPC and Section 2 of the PIL state that lisdexamfetamine should only be used during pregnancy if the potential benefit justifies the potential risk to the foetus, as determined by the doctor. Legal status - Medicinal product subject to restricted medical prescription. **Additional risk minimisation measures:** Checklist 1: Prescriber checklist before prescribing lisdexamfetamine Checklist 2: Prescriber checklist for ongoing monitoring during lisdexamfetamine treatment Chart for ongoing monitoring during lisdexamfetamine treatment